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EFFECT OF SERUM GONADOTROPIN AND CHORIONIC GONADOTROPIN ON THE HUMAN OVARY

ERIK RYDBERG, M.D.
AND
K. PEDERSEN-BJERGAARD, PH.D.
COPENHAGEN, DENMARK

At present, therapeutic experiments are carried out almost exclusively with two kinds of gonadotropic preparations, namely one prepared from the serum of pregnant mares and one derived from the urine of pregnant women.

In animal experiments the active principle prepared from the serum of pregnant mares—which in this paper will be designated as serum gonadotropin—has proved to stimulate the maturing of the ovarian follicles and to produce ovulation and the formation of corpus luteum.

The principle prepared from the urine of pregnant women appears to be formed in the placenta and will be designated as chorionic gonadotropin. In animal experiments its effect has differed with the species examined. From the observations reported so far it appears that chorionic gonadotropin in rodents, through cooperation with the pituitary of the animal, is able to produce a reaction similar to that obtained with serum gonadotropin. It is this effect that forms the basis for the Aschheim-Zondek test for pregnancy. In hypophysectomized animals an entirely different effect has been observed, namely luteinization of the theca without any maturing of follicles or corpus luteum formation. In experiments on monkeys, Engle [1] found that chorionic gonadotropin, in contrast to what might be expected, has an inhibitory effect on the ovarian function, and he even found regressive changes in the ovaries after such treatment.

Experimental studies have been carried out on human beings with both of the aforementioned gonadotropic principles. The substance was given to patients who were to be operated on, and subsequently the ovaries were examined at the operation—or, in some instances, an ovary was removed for microscopic examination.

The action of serum gonadotropin was studied in this way by Westman,[2] who found that the substance stimulates the development of the follicles and leads to a cystic enlargement of them, whereas it does not produce rupture of the follicles or formation of corpus luteum.

Also Watson, Smith and Kurzrok,[3] employing injection of the same preparation as that used by Westman, found cystic changes in the follicles and luteinization of the theca and, exceptionally, of the granulosa too.

Davis and Koff [4] were able by intravenous injection of serum gonadotropin to produce ovulation and formation of corpus luteum as well as maturing of the follicles. These observations have been confirmed by Siegler and Fein.[5]

Similar experiments have been carried out with chorionic gonadotropin. Hamblen and Ross [6] found no effect from this treatment on the human ovary. Nor was Westman [7] able to see any distinct effect from the injection of chorionic gonadotropin alone; in several instances, on the other hand, in which he first treated the patient with serum gonadotropin and subsequently with chorionic gonadotropin he found changes which he interpreted to indicate that the first substance had produced a ripening of the follicles which later went on to luteinization elicited by the chorionic gonadotropin.

Therapeutic experiments in cases of ovarian dysfunction have given rather divergent results. Positive results have been reported following treatment of amenorrhea both with serum gonadotropin [8] and with chorionic gonadotropin,[9] besides in combined treatment with these two substances (Rydberg,[9] Rydberg and Østergaard,[9] MacGregor [10] and Westman [11]).

Other authors have warned strongly against the employment of the gonadotropic substances in the therapy, and in June 1940 the Council on Pharmacy and Chemistry of the American Medical Association [12] published a report in which it said in conclusion that the treatment of ovarian disturbances with chorionic gonadotropin for the present has no rational foundation.

In recent years in the University Clinic of Gynecology, Copenhagen, we have carried out some experi-

From the University Clinic of Obstetrics and Gynecology, Copenhagen, Professor Rydberg, Chief.

1. Engle, E. T.: Gonadotrope Stoffe im Blut, Harn und in anderen Körperflüssigkeiten, Arch. f. Gynäk. **166:** 131-167, 1938.

2. Westman, A.: Untersuchungen über die Wirkung des gonadotropen Hypophysenvorderlappenhormones "Antex" (Leo) auf die Ovarien der Frau, Acta obst. et gynec. Scandinav. **17:** 492-515, 1937.

3. Watson, B. P.; Smith, P. E., and Kurzrok, Raphael: The Relation of the Pituitary Gland to the Menopause, Am. J. Obst. & Gynec. **36:** 562-570 (Oct.) 1938.

4. Davis, M. E., and Koff, K.: The Experimental Production of Ovulation in the Human Subject, Am. J. Obst. & Gynec. **36:** 183-199 (Aug.) 1938.

5. Siegler, L. S., and Fein, M. J.: Studies in Artificial Ovulation with Hormone of Pregnant Mares' Serum, Am. J. Obst. & Gynec. **38:** 1021-1036 (Dec.) 1939.

6. Hamblen, E. C., and Ross, R. A.: Responses of Human Ovary to Gonadotropic Principles, Endocrinology **21:** 722-726 (Nov.) 1937.

7. Westman, A.: Ueber den Luteinisierungseffekt des gonadotropen Chorionhormons auf die Ovarien der Frau, Acta path. et microbiol. Scandinav., 1938, supp. 37, pp. 567-577. Footnote 11.

8. Siegler, L. S.: Further Experiences with the Hormone of Pregnant Mare Serum, Endocrinology **27:** 387-391 (Sept.) 1940.

9. Rydberg, Erik: Einige Fälle von Metropathia haemorrhagica und sekundärer Amenorrhoe behandelt mit gonadotropem Hormon, Acta obst. et gynec. Scandinav. **18:** 1-23, 1938. Rydberg, Erik and Østergaard, E.: The Effect of Gonadotropic Hormone Treatment in Cases of Amenorrhea, Acta obst. et gynec. Scandinav. **19:** 222-246, 1939.

10. MacGregor, T. N.: Amenorrhea: Its Etiology and Treatment, Brit. M. J. **1:** 717-722 (April) 1938.

11. Westman, A.: Die gonadotropen Hormone und ihre therapeutische Anwendung, Geburtsh. u. Frauenh. **2:** 595-610 (Dec.) 1940; Die hormonale Behandlung der Amenorrhoen, Acta obst. et gynec. Scandinav. **21:** 105-150, 1941.

12. Chorionic Gonadotropin, Report of the Council on Pharmacy and Chemistry, J. A. M. A. **114:** 2306-2307 (June 8) 1940.

ments with gonadotropic substances along various lines; an account of them has been given in several publications.[9]

The present work will deal with our observations as to the dosage and combination of serum gonadotropin and chorionic gonadotropin preparations, and as to the immediate effect on the functions of the ovary in cases of amenorrhea.

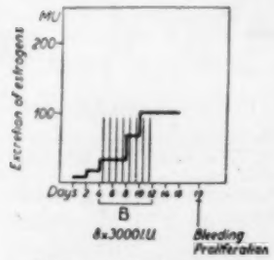

Chart 1.—Case of amenorrhea treated with chorionic gonadotropins. In the charts *A* shows dosage of serum gonadotropin and *B* of chorionic gonadotropins.

The general indications for treatment and the permanent results obtained will not be dealt with here, but the reader is referred to the paper by Rydberg and Østergaard[9] of 1939 in which our material at that time is described and classified from clinical points of view.

In the first therapeutic experiments performed by one of us (Rydberg) only chorionic gonadotropin was employed. As a rule, 1,500 international units was injected twice a week, and the treatment was continued for several weeks. About one half of the patients treated in this way reacted with bleeding, and on microscopic examination the endometrium was found to be in the secretory phase. From the studies on this material there could be no doubt that chorionic gonadotropin alone in certain cases of amenorrhea was capable of producing true menstruation.

Owing to the experimental experiences gained in the following period, we subsequently adopted a combined method of treatment, commencing with serum gonadotropin and continuing with chorionic gonadotropin. This form of treatment proved more effective, at least as far as the immediate effect is concerned, and hence we have continued with this method. If the doses given were sufficiently large, this combined treatment was capable in a majority of cases of secondary amenorrhea to establish a really complete cycle; in many of these cases the restored ovarian function kept on also after discontinuance of the treatment.

With the experiences gained in this way, various questions arose concerning the mode of action of these preparations and their expedient administration in therapy—questions that suggest themselves but often are difficult to answer, since clinical experimentation implies a good many considerations that are absent in experiments on animals, and it thus takes a longer time to gather sufficient experiences for definite conclusions.

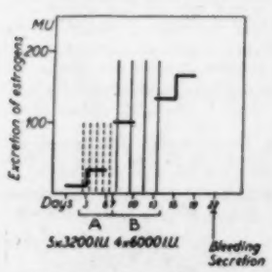

Chart 2.—Case of amenorrhea treated with serum and chorionic gonadotropins.

It has already been pointed out that the gonadotropins have various actions in different kinds of animals and that the opinions of their action in the human being still are highly divergent. Naturally the fact that a given type of treatment in a number of cases results in the effect desired is not a sufficient basis for conclusions as to the mechanism of the effect of the gonadotropic preparations employed. Real insight into the action of these substances may be gained only through accurate analysis of the cases under treatment and determination of the hormone excretory products that are characteristic of the two phases of the ovarian cycle, together with examination of the endometrium at the proper periods of time.

Some diagrams are presented of hormone-analytic records and therapeutic measures in a number of cases of amenorrhea in which rather thorough examinations have been made; in connection with the diagrams we shall present our conclusions as to the mode of action of the preparations employed and the dosage required. The cases here reported are selected from a large number of cases of amenorrhea; the total material will be worked up subsequently according to the clinical angle.

THE HORMONE ANALYSIS AND THE PREPARATIONS EMPLOYED

In the studies here reported, quantitative determination was made of the estrogenic substances in the urine before and during the treatment, besides, in several cases, of pregnandiol under the treatment.

The excretion of estrogens was determined prior to the institution of treatment and throughout the treatment with gonadotropic substance in order to ascertain a possible ovarian stimulation. We have determined

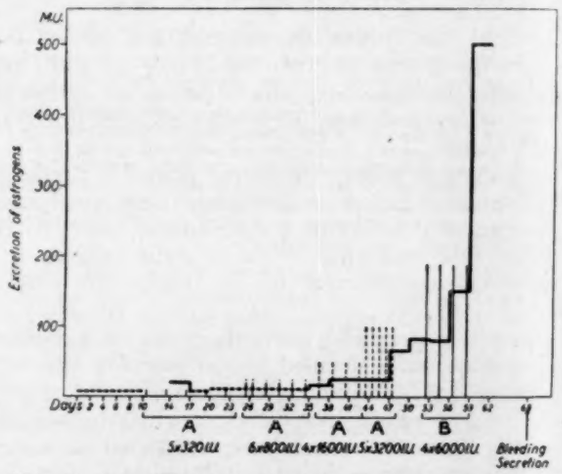

Chart 3.—Case of amenorrhea treated with serum and chorionic gonadotropins.

the content of estrogenic substances in the urine after the method given by Kemp and Pedersen-Bjergaard[13] with this modification: that the congo-acid urine before benzene extraction is mixed with an additional 80 cc. of concentrated hydrochloric acid per thousand cubic centimeters of urine, so that the ensuing heating causes hydrolysis of possibly combined forms of estrogenic substances. The extracts containing the total estrogenic activity were dissolved in oil and titrated on adult castrated female mice. In normal menstrual cycles the output of estrogens demonstrated after this method is from 15 to 150 mouse units per twenty-four hour output of urine.

In some of our cases we have further determined the output of pregnandiol during the treatment in order to ascertain a possible luteinization of the ovaries. As is well known, pregnandiol is an excretion product of progesterone, isolated first by Venning and Browne[14] as sodium pregnandiol glycuronate. The same authors[15] have later shown that pregnandiol is excreted normally during the latter half of the intermenstruum, i. e. in the

13. Kemp, T., and Pedersen-Bjergaard, K.: Ueber die Aufnahme- und Ausscheidungsverhältnisse des Follikulins beim Menschen, Endokrinologie **13**: 156-167, 1933.

14. Venning, E. M., and Browne, J. S. L.: Isolation of Water Soluble Pregnandiol Complex from Human Pregnancy Urine, Proc. Soc. Exper. Biol. & Med. **34**: 792-793 (June) 1936.

15. Venning, E. M., and Browne, J. S. L.: Studies on Corpus Luteum Function: Urinary Excretion of Sodium Pregnandiol Glucuronidate in Human Menstrual Cycle, Endocrinology **21**: 711-721 (Nov.) 1937.

corpus luteum phase. We have determined the amount of sodium pregnandiol glycuronate in the urine gravimetrically after Venning's[16] method, this substance being shaken out of the urine by means of butyl alcohol, recrystallized by means of acetone, dried and weighed. Pregnandiol itself, which has about the same molecular weight as progesterone, makes up about 60 per cent of the glycuronate. The values given for excretion of pregnandiol in charts 9 to 14 are calculated from the values obtained for the glycuronate output. In women with normal menstruation the pregnandiol output determined after this method is stated not to exceed 8 mg. in twenty-four hours.

The values recorded in the charts for estrogens and pregnandiol show the twenty-four hour output; they are averages of the excretions for two to three days, as a rule, as is evident from the graphs. The analyses were carried out in the biologic laboratory of Løvens kemiske Fabrik under the direction of one of us (Pedersen-Bjergaard). The preparations here employed are (1) serum gonadotropin and (2) chorionic gonadotropin prepared by "Løvens kemiske Fabrik."

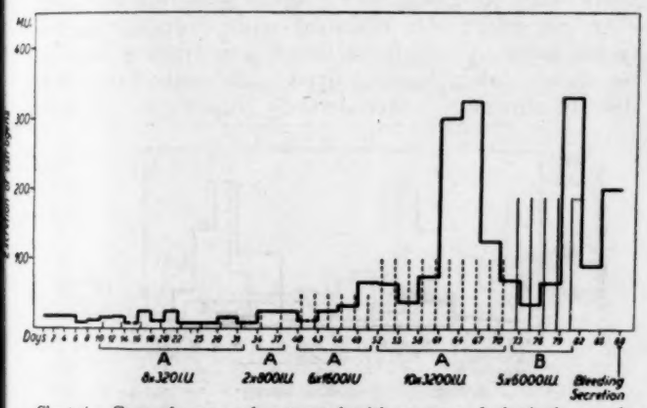

Chart 4.—Case of amenorrhea treated with serum and chorionic gonadotropins.

Both preparations are perfectly free from estrogens. Both are standardized by comparison with the international standard preparation, and the potency is given in international units.[17]

GRAPHIC PRESENTATION OF SOME TREATED CASES OF AMENORRHEA: COMMENTS

Explanation of the Signs in Charts 1 to 8.—The stepped curve gives the estrogen output in the urine per day in mouse units. When this curve is drawn in a dotted line it means that the actual values were not determined and that at any rate they fall below the value indicated by the dotted line. The dotted line to the extreme right in chart 7 (in continuation of the unbroken line) indicates that here it was not possible to follow the usual scale of the ordinate because of the very high values in this section. The vertical dotted line indicates injection of serum gonadotropin in international units and the vertical solid line injection of chorionic gonadotropin in international units.

Charts 1 and 2 illustrate two successive treatments of the same patient—a patient with primary amenorrhea. First she was given chorionic gonadotropin alone and in a subsequent treatment she was first given serum gonadotropin and, after this, chorionic gonadotropin.

In this case, as will be noticed, the treatment with chorionic gonadotropin alone, 24,000 international units, resulted in a decided increase in the output of estrogens, and a bleeding appeared after the discontinuance of

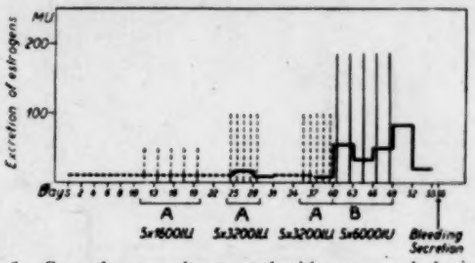

Chart 5.—Case of amenorrhea treated with serum and chorionic gonadotropins.

the treatment. At this time, however, the endometrium was only in the proliferation phase. From these results the only conclusion is that the chorionic gonadotropin in this case when given alone had a follicle stimulating effect but no luteinizing.

It has already been pointed out that the follicle stimulating effect of this principle is characteristic of the rodents, while it has not been practicable by direct examination to ascertain any follicle stimulating effects on the ovaries of patients receiving this treatment. In a few other cases too we have seen chorionic gonadotropin alone able to produce bleeding from the endometrium in the phase of proliferation.

Now we have more effective methods for adequate stimulation of the ovary, and we presented chart 1 merely because it illustrates the fact that the chorionic gonadotropin may act exclusively as a follicle stimulating agent.

Subsequently the same patient was treated first with serum gonadotropin and later with chorionic gonadotropin (chart 2). Also this treatment resulted in a considerable increase in the output of estrogens and bleeding, but this time the endometrium had undergone the clear premenstrual change at the appearance of the bleeding.

Charts 3 and 4 illustrate therapeutic experiments in which the treatment commenced with relatively small

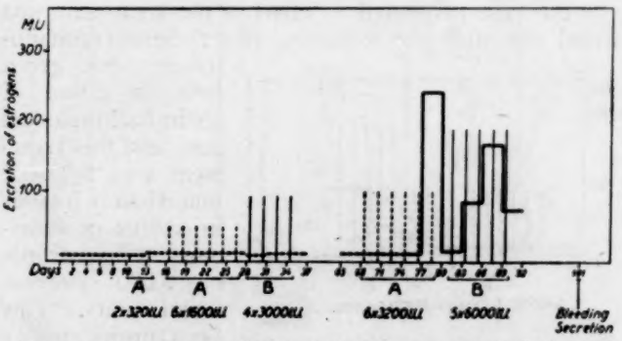

Chart 6.—Case of amenorrhea treated with serum and chorionic gonadotropins.

doses of serum gonadotropin; the dose was then increased slowly, after which chorionic gonadotropin was given, four or five injections of 6,000 international units. Here the excretion of estrogens does not rise distinctly until large doses of serum gonadotropin are given; 1,600 to 3,200 international units. The following treatment with chorionic gonadotropin produces an additional rise in the excretion of estrogens in the

16. Venning, E. M.: Further Studies on Estimation of Small Amounts of Sodium Pregnandiol Glucuronidate in Urine, J. Biol. Chem. **126**: 595-602 (Dec.) 1938.

17. Memorandum on the International Standard for the Gonadotropic Substance of Pregnant Mares' Serum, Bull. Health Organ., League of Nations **8**: 898-900, 1939. Memorandum on the International Standard for the Gonadotropic Substance of Human Urine of Pregnancy; Chorionic Gonadotropin, Bull. Health Organ., League of Nations **8**: 884-886, 1939.

first case; the other case shows at this moment a secondary rise in the excretion of estrogens after a fall coincident with the last injections of serum gonadotropin. In both cases there was bleeding from the mucosa at the stage of secretion a few days after the discontinuance of the treatment with chorionic gonadotropin. The results indicate that in stimulating treatment with serum gonadotropin the dose should not be less than about 2,000 to 3,000 international units per injection and that several such injections should be given in succession. As far as may be judged from the present cases, this form of treatment is follicle stimulating, but, as will be pointed out later, the treatment with serum gonadotropin is not sufficient to produce the complete ovarian cycle.

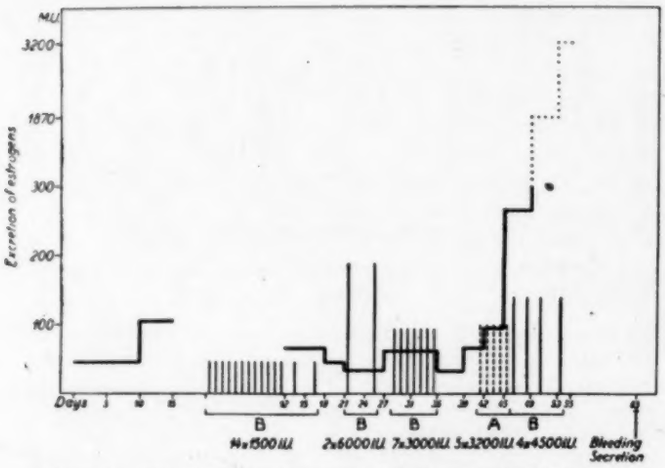

Chart 7.—Case of amenorrhea treated with serum and chorionic gonadotropins.

Chart 5 shows about the same results. In this instance a pause of some days was made between the three series of injections of serum gonadotropin, each of five injections. After the last injection of serum gonadotropin chorionic gonadotropin was given in the usual manner. A distinct rise in the excretion of estrogens was first demonstrated at the beginning of chorionic gonadotropin therapy, the rise most likely in the beginning, however, being due to the serum gonadotropin therapy. The combined treatment was followed by menstruation.

In the case presented in chart 6 the treatment was carried out after the following plan: Serum gonadotropin was given first in doses of about half the usual size, and this treatment was followed immediately by four injections of chorionic gonadotropin of 3,000 international units. This treatment gave neither any rise in the excretion of estrogens nor any bleeding. After a pause of one month the patient was given a new series of serum plus chorionic gonadotropin, and this time the doses of both preparations were doubled. The last series of injections brought about both a rise in the excretion of estrogens and menstruation. This case confirms the view that in the serum gonadotropin therapy the dose should be at least 2,000 to 3,000 international units per injection. It is to be emphasized that the negative result of the first treatment in this case is not due to insufficiency of chorionic gonadotropin dosage, for we have found that after treatment with sufficient doses of serum gonadotropin an adequate response to injections of chorionic gonadotropin is obtained regularly when considerably smaller doses are given than those employed here. The question about the proper dosage of chorionic gonadotropin will be dealt with later. In these cases the main object was to find a suitable administration of serum gonadotropin in the combined therapy. The cited cases show, then, that five consecutive injections of 3,000 international units of serum gonadotropin seem to constitute a rational procedure when the aim is to stimulate the follicular activity in cases of failing or lowered ovarian function.

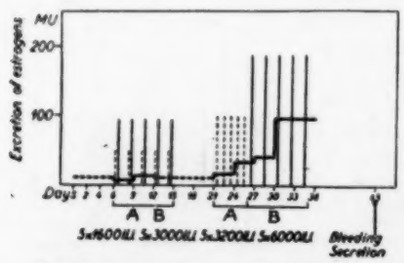

Chart 8.—Case of amenorrhea treated with serum and chorionic gonadotropins.

Chart 7 illustrates a therapeutic experiment in a case of amenorrhea in which the output of estrogens prior to the treatment kept at an entirely normal level. Here we commenced with chorionic gonadotropin therapy alone—which perhaps would seem quite rational in such a case—since, according to experimental studies on man and animals, the chorionic hormone should act particularly as a luteinizing agent. In this case, however, no effect was obtained with chorionic gonadotropin alone, although the doses here employed, as will be shown later, have proved sufficiently large when this treatment is preceded by injections of serum gonadotropin. The usual combined treatment resulted in an enormous rise in the output of estrogens and menstruation. Naturally this experiment may be interpreted in various ways, but at any rate it illustrates clearly the effectivity of the combined treatment.

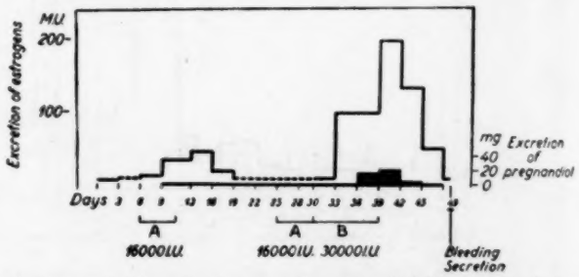

Chart 9.—Excretion of estrogens and pregnandiol in the urine in a case of amenorrhea treated with serum and chorionic gonadotropins.

Chart 8 presents a therapeutic experiment in which serum and chorionic gonadotropin first were given together, without any distinct effect. Then the usual successive treatment with the two preparations was given and resulted in an increased excretion of estrogens and menstruation.

This sort of experiment might indeed be varied with differing dosages, but we did not consider it likely to result in any advance.

As mentioned in the introductory remarks, some authors have made observations indicating a possible luteinizing effect of the serum gonadotropin on the human ovary. This effect, if constant, would mean that this principle alone would be sufficient to produce a complete ovarian cycle and that the following chorionic gonadotropin therapy thus would not be required.

In order to see whether treatment with serum gonadotropin alone might possibly be able to replace our combined method, we gave 4 patients a preliminary treatment with 16,000 internatioinal units of serum gonadotropin, and after a pause of two weeks or a little longer we gave them our usual combined treatment, commencing with the same number of injections

of serum gonadotropin in the same doses as before and continuing with the administration of 30,000 international units of chorionic gonadotropin. During this treatment we have followed the excretion of estrogens in the urine and have also determined the output of pregnandiol. The presence of pregnandiol in the urine shows that corpus luteum is formed. The absence of pregnandiol does not perhaps indicate with absolute certainty that corpus luteum is not formed, as according to our experiences it is difficult with accuracy to determine the small amounts of this substance that correspond to the normal cycle. From charts 9 to 12, however, it is evident that the appearance of the bleedings, the condition of the endometrium and the amount of pregnandiol demonstrated in the urine clearly show the difference in the effect of serum gonadotropin alone and of serum and chorionic gonadotropins combined.

Explanation of the Signs in Charts 9 to 12.—As in the preceding charts, the stepped curve gives the output of estrogens per day in mouse units. The unbroken line on the abscissa indicates that the excretion of pregnandiol was assayed but pregnandiol was not present in any measurable amount. The black rectangular areas on the abscissa give the output of pregnandiol in milligrams per day.

Chart 9 illustrates a therapeutic experiment after the plan already given. The serum gonadotropin therapy produced a minor rise in the excretion of estrogens but no bleeding or any measurable output of pregnandiol. Treatment with serum and chorionic gonadotropins was followed by a greater excretion of estrogens, and a considerable amount of pregnandiol was found in the urine during and after the injections of chorionic gonadotropin; a few days later menstruation appeared.

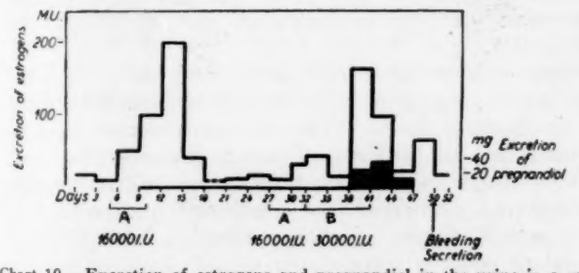

Chart 10.—Excretion of estrogens and pregnandiol in the urine in a case of amenorrhea treated with serum and chorionic gonadotropins.

Chart 10 illustrates the treatment in a case after the same lines as given in chart 9. The reaction is essentially the same.

In chart 11 a similar effect is seen with regard to the excretion of estrogens and pregnandiol. In this case there was a little bleeding after the serum gonadotropin therapy, but a specimen of the endometrium showed this to be in the proliferative phase, though exhibiting slight cystic hyperplastic changes. After the combined treatment a new bleeding appeared, and this time the mucous membrane was in the premenstrual phase.

In the experiment portrayed in chart 12 a trace of pregnandiol could be demonstrated in the urine after the first series of injections of serum gonadotropin alone. The appearance of bleeding at this time caused a specimen of the endometrium to be taken; this was found to be in the proliferative stage and showed no sign of secretion. The demonstrated trace of pregnandiol allows of no definite conclusion. Perhaps there was a beginning luteinization, but at any rate this has not been sufficient to bring the endometrium into the secretory phase. The subsequent combined therapy had the typical effect.

In recapitulation of the experiences from the therapeutic experiments here described—to which could be added a long series of cases confirming the results

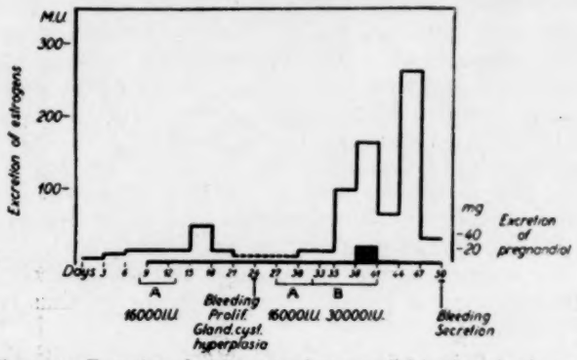

Chart 11.—Excretion of estrogens and pregnandiol in the urine in a case of amenorrhea treated with serum and chorionic gonadotropins.

reported—it may be said that an adequate stimulation of the human ovary, by inhibited function, to an activity similar to the normal spontaneous process, i. e., beginning with follicular stimulation and going on to luteinization, is best obtained by a combined treatment commencing with serum gonadotropin and continuing with chorionic gonadotropin. We found the suitable dosage of serum gonadotropin to be about 3,000 international units daily for some days in succession—for instance, five days. Then chorionic gonadotropin is to be employed.

It now remains to look into the dosage of chorionic hormone required for the production of luteinization, as the therapeutic experiments reported tell nothing about the minimal dose of chorionic gonadotropin that with reasonable regularity produces luteinization after a preceding treatment with serum gonadotropin.

In order to elucidate this question, we have treated a series of patients first with the dose of serum gonadotropin (3,000 international units × 5) we found suitable according to the preceding experiments and then

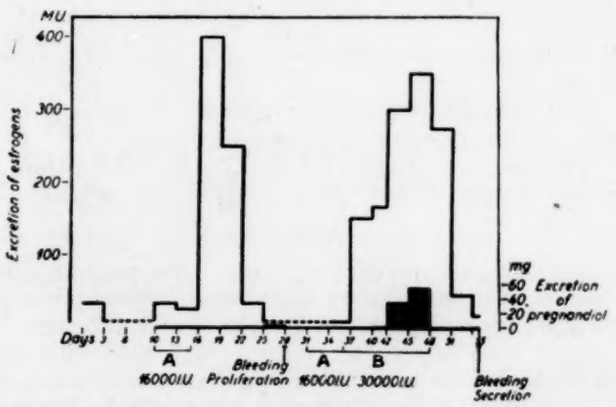

Chart 12.—Excretion of estrogens and pregnandiol in the urine in a case of amenorrhea treated with serum and chorionic gonadotropins.

with chorionic gonadotropin in different doses, as recorded in the accompanying table.

The first column gives the number of reactors, i. e. patients responding to the treatment with a distinct increase in output of estrogens. In this table we have included only such reactors, leaving out a small number of patients who proved quite refractory to the stimulation with gonadotropic substances. Since the

question looked into here is the proper dosage of chorionic gonadotropin required for the production of luteinization after a preceding adequate follicular stimulation with serum gonadotropin, the entirely refractory cases have to be left out of consideration.

As will be seen from the table, any dosage of serum gonadotropin under 1,500 international units × 3 is undoubtedly inadequate. With this chorionic gonadotropin dosage of 1,500 international units × 3 we obtained a complete reaction (i. e., bleeding from a mucous membrane in typical premenstrual phase) in 10 out of 12 cases. In 1 case bleeding was obtained but the mucous membrane was not of the premenstrual type, and in another case no bleeding appeared, but a definite excretion of pregnandiol has to be looked on as indicating that luteinization has taken place.

We stopped at the last dosage, and the method for administration of gonadotropic substance we thus have arrived at is as follows:

Serum gonadotropin, 3,000 international units daily for five consecutive days, then chorionic gonadotropin

Reaction of Amenorrheic Patients on Various Doses of Chorionic Gonadotropin Given After Preliminary Treatment with Serum Gonadotropin (3,000 International Units × 5)

	Number of Reactors	No Bleeding	Bleeding, but Mucosa Not in Premenstrual Phase	Bleeding, Premenstrual Mucosa
1. Chorionic gonadotropin 3 × 100 international units after preceding treatment with serum gonadotropin	5	1	4 (1 in secretion but not premenstrual; 3 without signs of secretion)	0
2. Chorionic gonadotropin 3 × 250 international units after preceding treatment with serum gonadotropin	7	2	3	2
3. Chorionic gonadotropin 3 × 500 international units after preceding treatment with serum gonadotropin	10	2	5 (1 in secretion but not premenstrual; 4 without signs of secretion)	3
4. Chorionic gonadotropin 3 × 1,500 international units after preceding treatment with serum gonadotropin	12	1 (Pregnandiol : +)	1 (Pregnandiol : 0)	10

1,500 international units every other day, three times in all.

The menstruation usually appears about ten days after the last injection of chorionic gonadotropin.

The last two graphs, charts 13 and 14, illustrate a couple of cases in which this dosage was employed.

COMMENT

It would fall outside the scope of this paper to discuss in detail the clinical questions connected with the therapeutic employment of gonadotropic substances.

Here it is merely to be mentioned that with this method we have been able to produce menstruation in a greater majority of our patients with secondary amenorrhea and in some patients with primary amenorrhea, and that, according to our present experiences, about one half of the patients treated in this way have continued menstruating after the treatment. We have now seen many instances of striking, truly favorable therapeutic results—for instance, pregnancy in 2 cases of primary amenorrhea and continued regular menstruation in many cases of secondary amenorrhea; also some instances of pregnancy after the treatment of secondary amenorrhea.

The treatment may give some untoward effects, the most important of which is the not altogether infrequent production of a considerable swelling of one of the ovaries or of both. The patient may then have a sensation of tension or of pain in the abdomen, and on palpation the ovary is found to be enlarged, so that it may even rise from the pelvis like ovarian cysts. Usually no great inconvenience results from this complication; the patient has to keep to her bed for a few days and then this reaction subsides rapidly. In 1 case we were able during a laparotomy to ascertain that it was a matter of lutein tumors. In this case there was an unusually strong abdominal reaction, and since we were not familiar with this effect of the treatment we thought that there were indications for the performance of a laparotomy.

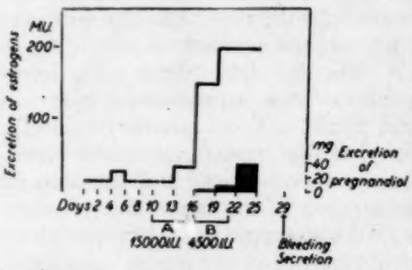

Chart 13.—Course of a case of amenorrhea treated with serum plus chorionic gonadotropins as given in the text.

A transitory rise in temperature is not infrequent. Serum gonadotropin is less active in this respect, but chorionic gonadotropin gives not infrequently a brief elevation of the temperature to 38-39 C. (100.4-102.2 F.).

The undesirable effects mentioned have not been so bad as to keep us from giving ambulatory treatment in a good many cases. The ovarian reaction just mentioned has to be kept in mind, however, as such a lutein tumor and the resulting symptoms may easily be mistaken for other morbid conditions, and patients with any severe degree of such a reaction have to be confined to bed for some days.

SUMMARY

In cases of failing ovarian function in women, the gonadotropic preparations can produce an adequate reaction in the ovary followed by menstruation. By a suitable dosage it is practicable in most cases of secondary amenorrhea to set the ovarian function going at least temporarily and often permanently.

It was found most expedient to treat the patients first with serum gonadotropin and afterward with chorionic gonadotropin.

Experimental studies led to a rational dosage and a standard method for this stimulation therapy: Intramuscular injection of 3,000 international units of serum gonadotropin is given daily for five consecutive days and then 1,500 international units of chorionic gonadotropin is given every day, three times in all.

In reacting patients the menstruation makes its appearance about ten days after the last injection.

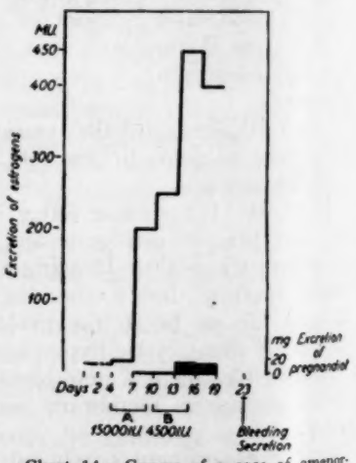

Chart 14.—Course of a case of amenorrhea treated with serum plus chorionic gonadotropins as given in the text.

ADJUNCTIVE THERAPY WITH DIETHYLSTILBESTROL IN OBSTETRICS AND GYNECOLOGY

CRITICAL EVALUATION

A. R. ABARBANEL, M.D.
WASHINGTON, D. C.
HARRY ARANOW, M.D.
AND
MILTON J. GOODFRIEND, M.D.
NEW YORK

Before proceeding to evaluate the present status of diethylstilbestrol in clinical obstetrics and gynecology, let us observe where diethylstilbestrol fits into our therapeutic philosophy by briefly reviewing certain significant trends in reproductive physiology, especially as regards our conception of the so-called "sex" hormones estradiol, progesterone and testosterone. The guiding principle in these recent advances has been the premise that all biologic processes are essentially chemical in nature.

Basic in its significance was the demonstration that the steroid nucleus is not essential for gynecologic activity, because its implications are so broad and sweeping. In a series of investigations that forms one of the most fascinating chapters in modern medical annals, Dodds [1] and his co-workers chemically dissected the steroid skeleton of estradiol in a search for the chemical moiety requisite for gynecogenic activity. Among the scores of nonsteroidal chemical substances evolved, a very potent gynecogen was discovered in 4-4′-diethyldihydroxy-stilbene, popularly known as stilbestrol, but for which the designation diethylstilbestrol, recommended by the Council on Pharmacy and Chemistry of the American Medical Association, will be used throughout this report. Pharmacologically, diethylstilbestrol is essentially similar to estradiol in every important respect but one. Diethylstilbestrol loses little of its potency when administered orally, because, unlike estradiol, it is not inactivated by the liver.[2]

Important also have been the findings of the biologist that each of these so-called sex hormones, as well as diethylstilbestrol, possesses bisexual properties.[3] Since not one of them is specific for either sex, one can no longer logically retain such terms as "male sex hormone" or "female sex hormone," for, by definition, such entities do not exist.[4] Each exerts both androgenic and gynecogenic activity.[5]

Equally significant have been the contributions of the physiologist and pharmacologist in showing that these so-called sex hormones, as well as diethylstilbestrol, may materially influence many diversified phases of the body economy of both the male and the female independent of any effects on the secondary sexual apparatus.[6] In short, so great is the weight of the evidence that no one can any longer consider the genital tract as a periscope with which to view the extragenital effects of diethylstilbestrol, estradiol, progesterone or testosterone. Rather, one must recognize that these chemical substances possess multiple constitutional activities that are not dependent on their effects on the secondary sex organs.

In review, then, it is noted that the nonsteroidal chemical substance diethylstilbestrol is a constitutional drug. In its influence on the secondary sexual apparatus it exhibits bisexual activity, although its properties are preponderantly gynecogenic. Since the latter were the first to be recognized, diethylstilbestrol at present has found its widest use in clinical obstetrics and gynecology, especially since it is efficacious orally as well as relatively inexpensive. Growing recognition of its multiple constitutional effects, however, has brought about its introduction in several other fields, such as internal medicine, otorhinolaryngology, dermatology and dentistry.

Now let us note where diethylstilbestrol fits into our general plan of therapy. An adequate therapeutic regimen must include treatment of the entire patient, the sum of her mental as well as physical ills, be they real or imaginary. Treatment has to be individualized because each patient presents problems peculiar to herself. Furthermore, gynecic endocrinopathies in their basic concept represent disturbances in the metabolism of the endocrine glands themselves or of the recipient organs or both. Since each patient is the metabolic sum of what she eats and drinks, it becomes clear why diet and thyroid are of fundamental importance in gynecic endocrine therapy. A diet to be adequate must not only be properly balanced but also be properly cooked so as to preserve the essential vitamins and minerals.[7] Caloric intake, in comparison, is of secondary importance.[8] Thyroid exerts a profound stimulating influence on the general metabolic functions of the organism.[9]

Equally important in the management of the patient is mental readjustment and reassurance. The physician must sweep away the cranial cobwebs spun by the spiders of folklore and superstition, especially with

From the Department of Obstetrics and Gynecology, Morrisania Hospital, New York.

Diethylstilbestrol-monomethyl-ether (Monomestrol) was supplied by Wallace & Tiernan Products Company.

Owing to lack of space, this article has been abbreviated for publication in THE JOURNAL. The complete article appears in the authors' reprints.

Testosterone propionate and methyl testosterone were supplied as Perandren and Metandren respectively by Ciba Pharmaceutical Products, Inc.

Dr. Abarbanel is now associated with the Department of Obstetrics and Gynecology of George Washington University School of Medicine, Washington, D. C.

Read before the Section on Obstetrics and Gynecology at the Ninety-Third Annual Session of the American Medical Association, Atlantic City, N. J., June 10, 1942.

Diethylstilbestrol was supplied as Estrobene by Mr. A. A. Ebby of Ayerst, McKenna and Harrison, Ltd., and as Stilbestrol-Squibb by Dr. J. A. Morrell of E. R. Squibb & Sons.

1. Dodds, E. C.: Stilbestrol, Practitioner **142**: 309-313 (March) 1939.

2. Zondek, Bernhard, and Sulman, Felix: Inactivation of Diethylstilbestrol in the Organism, Nature, London **144**: 596-597 (Sept. 30) 1939.

3. Korenchevsky, V.: Bisexual Properties and Cooperative Activity of Sexual Hormones and Their Effects on Females, Brit. M. J. **2**: 896-899 (Nov. 6) 1937. Jacobsen, E.: Die Wirkung von 4,4′ Dioxy-Diäthylstilben auf die Hypophyse gonadectomierter Ratten, Endokrinologie **21**: 20-24, 1938.

4. Abarbanel, A. R.: Rationale for the Use of Testosterone Propionate in Immediate Treatment of Excessive Uterine Bleeding, Am. J. Obst. & Gynec. **39**: 243-254 (Feb.) 1940.

5. The description of the action of any one of these chemical substances must be based on the specific effect of a particular substance on an individual and organ under a definite set of circumstances and then compared to what has been set up as the norm for maleness and for femaleness. If, under these conditions, the action is exerted in the direction of "maleness" it is called androgenic, while if it is in the direction of "femaleness" it is called gynecogenic. The gynecogens are further subdivided into estrogens, which bring about proliferative changes in the secondary sexual apparatus, and progestogens which cause maturation or progestational changes.

6. Reynolds, S. R. M.: Gynecic Physiology and the Gynecologist, Am. J. Surg. **48**: 175-196 (April) 1940.

7. If the services of an expert dietitian are not available, detailed information may be secured from the Bureau of Home Economics, Department of Agriculture, Washington, D. C.

8. McLester, J. S.: Nutrition and Diet in Health and Disease, ed. 3, Philadelphia, W. B. Saunders Company, 1939, chapter 13.

9. If the patient proves sensitive to thyroid, 10 to 15 drops of compound solution of iodine (Lugol's solution) or saturated solution of potassium iodide administered concurrently with the thyroid frequently helps offset the side effects.

regard to disorders of menstruation and their influence on sex. In addition, a critical analysis and adjustment of psychogenic factors deriving from marital, social or economic causes may often be essential for a successful therapeutic result.

A complete physical examination should always be performed by a competent internist preliminary to a thorough gynecologic examination which includes a speculum examination of the cervix. These should be repeated at frequent intervals.

Clearly, then, in the light of these considerations diethylstilbestrol, being but a single drug, can comprise just one adjunctive portion of a rational therapeutic regimen.

Proceeding on the general plan of therapy just outlined, the present status of the adjunctive use of diethylstilbestrol in clinical obstetrics and gynecology has been critically evaluated. This has been based mainly on our personal experience in over 700 cases (table 1).

TABLE 1.—*Various Conditions in Which Adjunctive Therapy with Diethylstilbestrol Was Employed*

Indication	General Management	Total Treated	General Management: Alone	General Management: Plus Diethylstilbestrol	Evaluation of Adjuvant Use of Diethylstilbestrol
Climacteric vasomotor instability	Mental reassurance, sedation, "score card" diet, thyroid	425	304	221	Excellent adjunctive value
Senile vulvovaginitis (including essential senile pruritus)	Establish diagnosis, diet, thyroid, acid douches, cotton tampons	32	14	18	Excellent adjunctive value
Juvenile vulvovaginitis (gonococcic)	Establish diagnosis, hygienic regimen, sulfonamides	21	0	21	Excellent adjunctive value
Puerperal painful, engorgement of breasts	Proper uplift, breast support				
Prevention		500	250	250	Excellent
Relief		100	50	50	Fairly good
Amenorrhea	Establish diagnosis, mental reassurance, diet, thyroid, repeated biopsies				Excellent ds aid in correcting mental maladjustment
Secondary		42	24	18	
Primary		6	2	4	Also physical disproportion
Induction of early abortion	Medical induction, potent oxytocics	24	..	24	No value whatsoever
Inhibition of onset of adequate milk secretion	Baby nursing	50	25	25	Value only temporary
Suppression of established lactation	Baby nursing	50	25	25	No value (actually stimulates lactation)
Galactorrhea		6	..	6	No value
Induction of premature labor	Medical induction, potent oxytocics	16	10 failed	10+6=16	Results only suggestive
Missed abortion or labor	Medical induction, potent oxytocics	4	4	4	Results quite suggestive
Uterine inertia (myometrial origin)	Establish diagnosis, sedation, fluids	10	10	10	Results only suggestive
Primary dysmenorrhea	Mental readjustment, diet, thyroid antispasmodics	21	21	21	Value very limited

In addition, we have fully utilized the extensive clinical literature as well as the personal communications of many investigators[10] in forming these conclusions. The detailed management of most of the conditions to be discussed may be found in several of the recent textbooks.[11] The physiologic considerations on which rational therapy is based has been clearly presented and adequately correlated by Reynolds.[12]

GROUP 1. CONDITIONS IN WHICH ADJUNCTIVE THERAPY WITH DIETHYLSTILBESTROL IS OF DEFINITE VALUE

1. *Climacteric.*—The climacteric may occur during or after the transition period at which reproductive function usually ceases. This phenomenon is a normal physiologic one, characteristic of the process of aging. In some individuals definite vasomotor instability may occur, noted clinically as hot flushes, sweats, chills or suffocations.[13] Although their exact etiology has never been clearly proved, it seems that these characteristic vasomotor phenomena appear to reflect an instability of the heat regulating mechanisms of the individual.[12] Any circumstance, physical or mental, which places a stress on the peripheral heat regulating apparatus will intensify those symptoms. Adjunctive therapy with diethylstilbestrol, as well as with estradiol or testosterone, helps bring about symptomatic relief by tending to stabilize heat regulating mechanisms through their action on the peripheral vascular tree. This is accomplished, according to Reynolds and his co-workers, in part by a direct action on the blood vessels themselves and in part indirectly through the central nervous system.[14]

The common sense management of these patients has been adequately described by Novak[15] and others. Certain points require added emphasis. Mental reassurance is of primary and paramount importance, for it is well established that the vasomotor phenomena of the climacteric may be deeply influenced by the patient's own psyche.[14] Accordingly, at the very first visit an attempt should be made to evaluate the entire patient, mentally as well as physically. Once the diagnosis is established, a frank discussion with the patient of her condition is essential in securing her complete confidence and cooperation as well as in ridding her of many erroneous apprehensions regarding the cessation of menstruation.

In addition, she is instructed to keep a daily written record noting separately the number of flushes observed during the day and the number experienced after retiring at night. Supportive treatment includes a well

10. Particularly Drs. R. R. Greene, M. E. Davis, C. V. MacBryde and K. J. Karnaky.

11. Novak, Emil: Gynecology and Female Endocrinology, Boston, Little, Brown & Co., 1941. Mazer, Charles, and Israel, S. L.: Diagnosis and Treatment of Menstrual Disorders and Sterility, New York, Paul B. Hoeber, Inc., 1941. Fluhmann, C. F.: Menstrual Disorders, Philadelphia, W. B. Saunders Company, 1939. Hamblen, E. C.: Endocrine Gynecology, Springfield, Ill., Charles C Thomas, Publisher, 1939.

12. Reynolds, S. R. M.: Physiology of the Uterus, with Clinical Correlations, New York, Paul B. Hoeber, Inc., 1939.

13. Maranon, Gregorio: The Climacteric, St. Louis, C. V. Mosby Company, 1929.

14. Reynolds, S. R. M.; Kaminester, Sanford; Foster, Frances I., and Schloss, Stewart: Psychogenic and Somatogenic Factors in the Flushes of the Menopausal Patient, Am. J. Obst. & Gynec. **41**: 1022-1028 (June) 1941.

15. Novak, Emil: The Management of the Menopause, Am. J. Obst. & Gynec. **40**: 589-595 (Oct.) 1940; Gynecology and Female Endocrinology.[11]

balanced diet [7] and the use of thyroid, especially if she is obese or tired and listless. Since bromides, in our experience, have proved far more effectual than barbiturates, 15 grains (1 Gm.) of triple bromides are prescribed three or four times daily. The patient is seen two weeks later. Her response may be evaluated from her story as well as from her "score card." If she has had no flushes at all during the night, the menopausal syndrome may be considered as mild or else the flushes probably stem from some psychogenic problem. Further careful sympathetic questioning should reveal the cause. If the patient is progressing satisfactorily, therapy is continued. In this manner it was found possible to control almost 50 per cent of over 400 menopausal patients. In other words, a little over 50 per cent (221 cases) required further adjunctive therapy with diethylstilbestrol.

The initial daily dose of oral diethylstilbestrol should range from 0.1 to 0.25 mg. and only enough to last two weeks should be prescribed.[16] Some investigators [17] prefer to start with a larger dose (1 mg.), but this is neither desirable nor necessary.[18] It is better to adjust the dose to the patient than the patient to a certain dosage. Depending on her response, the dose level may be maintained or increased by doubling the initial dose. The patient should then be seen at two week intervals and the dose level adjusted until she is in good equilibrium; that is to say, she is having no flushes at night and only an occasional one during the day. The dosage required to achieve equilibrium is maintained for a month or so before it is gradually lowered. The patient should be kept in equilibrium for a minimum of three to six months or more before discontinuing diethylstilbestrol in order to reduce the possibility of a recurrence of symptoms to a minimum. Under this regimen satisfactory relief was secured in over 92 per cent of our cases.

For patients still menstruating at more or less regular intervals, the daily oral dose should not exceed 0.5 mg. if troublesome bleeding is to be avoided. If 0.5 mg. is insufficient, it is expedient to add 10 to 20 mg. of oral methyl testosterone daily to the therapeutic regimen or else use this steroid alone. On the other hand, if a patient begins to bleed after an amenorrhea of one year or more a diagnostic biopsy or curettage should be done to rule out possible cancer.

In a very small minority it may be found necessary to give diethylstilbestrol by injection. Sesame oil should be the vehicle of choice. The initial dose should range from 0.2 to 0.5 mg. weekly.

Occasionally it may be necessary to employ the subcutaneous injection of a 10 mg. pellet of crystalline diethylstilbestrol. Before this is done, however, the patient must first show a satisfactory response to oral diethylstilbestrol. The pellet form of therapy yields the smoothest and best results per unit weight of any method of administration we have tried.[16]

2. *Essential Senile Vulvovaginitis, Including Essential Senile Pruritus.*—Since this syndrome is a part of the process of aging of the individual, the entire patient must be treated, not just one of her symptoms. Other constitutional and local causes must be excluded. Supportive treatment includes a well balanced, properly cooked diet, rich in vitamins and minerals, as well as small doses of desiccated thyroid. At first the patient is instructed to douche twice daily while lying flat on her back in the bathtub, using 2 quarts of a lukewarm solution containing 3 to 4 ounces of ordinary household vinegar.

If relief is not evident in two to four weeks, local therapy with an ointment containing 5 mg. of diethylstilbestrol per ounce is started, as this is the most effective and efficient means of administration.[19] Approximately enough ointment to contain 0.5 to 1.0 mg. of diethylstilbestrol is rubbed thinly over the vulva once a day, while a small amount is smeared lightly over a vaginal cotton tampon before the latter is inserted. Acid douches are continued. When kraurosis vulvae is pronounced, it may take several months to achieve complete relief. Pelvic examinations should be performed frequently to rule out a possible damming up of secretions, such as pyocolpos or hematometria.

Uterine bleeding may occur at infrequent intervals, but it rarely is alarming. Sufficient ointment to contain 4 to 8 mg. of testosterone may be substituted once or twice a day for one week out of every four. In fact, when the itching is extremely pronounced about the folds of the clitoris, testosterone ointment should be used daily, for this steroid seems to stimulate the surrounding glands to produce an oily secretion which serves to relieve the dry itching skin.[20]

3. *Juvenile (Gonococcic) Vulvovaginitis.*—After the diagnosis has been made by smear or culture, the mother is given careful detailed instructions regarding proper hygienic care of the child. A suppository containing 0.1 mg. of diethylstilbestrol is inserted vaginally each night. If the child strongly resents this method of administration, 0.1 mg. of oral diethystilbestrol may be given one to three times daily. By watching the weekly progress of the disease, the dosage may be maintained or raised. Sulfonamides may be included in the therapeutic regimen. Once the smears or cultures are negative for three consecutive weeks, diethylstilbestrol may be discontinued, although the child should receive a monthly checkup for at least six months.[21]

4. *Painful Engorgement of the Breasts in the Puerperium.*—This syndrome results from lymphatic and venous stasis, not from distention of the ducts with the milk.[22] By what means diethylstilbestrol may prevent or relieve this condition cannot be explained on the basis of our present day knowledge.[23] That it is not

16. Abarbanel, A. R., and Klein, M. D.: Clinical Experiences with Stilbestrol, New York State J. Med. **41:** 383-389 (Feb. 15) 1941.

17. Weed, J. C.; Weinstein, B. B.; Lock, F. R.; Douglas, J. W., and Collins, C. G.: The Oral Administration of Stilbestrol, Am. J. Obst. & Gynec. **39:** 1047-1049 (Oct.) 1940. Frank, R. T.; Goldberger, M. A., and Felshin, Gertrude: Clinical and Laboratory Investigations of Some of the Newer Sex Hormone Preparations, Endocrinology **27:** 381-384 (Sept.) 1940. Pratt, J. P.: A Clinical Study in Estrogenic Therapy, J. Clin. Endocrinol. **1:** 50-52 (Jan.) 1941.

18. Greene, R. R., and Dorr, E. M.: Relation of Dose and Type of Estrogen to Nausea and Vomiting, J. Clin. Endocrinol. **1:** 821-823 (Oct.) 1941. Mazer, Charles; Israel, S. L., and Ravetz, Elkin: The Synthetic Estrogen Stilbestrol, J. A. M. A. **116:** 675-681 (Feb. 22) 1941. MacBryde, C. M.; Castrodale, Dante; Loeffel, Ellen, and Freedman, Harold: The Synthetic Estrogen Diethylstilbestrol: Clinical and Experimental Studies, ibid. **117:** 1240-1242 (Oct. 11) 1941.

19. Finkler, R. S., and Antopol, William: Histological Changes in the Senile Vagina Induced by Estrogenic Therapy Administered Orally and by Inunction, Endocrinology **25:** 925-932 (Dec.) 1939. Greenblatt, R. B.; Torpin, Richard, and Brown, W. R.: Diethylstilbestrol: A Clinical Evaluation of the Various Modes of Administration, South. M. J. **33:** 1276-1285 (Dec.) 1940. Davis and Boynton.[27] Abarbanel and Klein.[16]

20. Hamilton, J. B.: Male Hormone Substance: Prime Factor in Acne, J. Clin. Endocrinol. **1:** 570-592 (July) 1941.

21. Karnaky, J. J.: Clinical Use of the New Synthetic Estrogenic Hormone Stilbestrol, South. M. J. **32:** 813-815 (Aug.) 1939. Russ, J. D., and Collins, C. G.: The Treatment of Prepuberal Vulvovaginitis with a New Synthetic Estrogen: Preliminary Report, J. A. M. A. **114:** 2446-2448 (June 22) 1940. Abarbanel and Klein.[16]

22. Abarbanel, A. R., and Goodfriend, M. J.: The Effects of Stilbestrol on Lactation, Am. J. Obst. & Gynec. **40:** 1037-1046 (Dec.) 1940.

23. Meites, Joseph, and Turner, C. W.: Studies Concerning the Mechanism Controlling the Initiation of Lactation at Parturition, Endocrinology **30:** 711-732 (May) 1942.

by inhibition of lactation has been clearly proved.[24] As a matter of fact, diethylstilbestrol, by stimulating a definitely increased production of lactogenic hormone by the anterior pituitary, actually promotes lactation.[23]

The management of painful engorgement resolves itself into two phases: (1) prevention and (2) relief after it comes on.[22] Every puerperal patient should be fitted with an adequate uplift breast binder that raises each breast up and mediad toward the opposite shoulder. It must fit snugly at the base and be very loose across the axillary portion of the breast. An old uplift brassière or a proper nursing brassière usually is quite satisfactory.

Prevention (in nonnursing mothers): An adequate uplift breast support is first adjusted on the patient. On the day of delivery, 10 mg. of oral diethylstilbestrol is given followed by 5 mg. daily for three to five days, then 3 mg. daily for three days and finally 1 mg. daily for three to six days. By spreading the dose schedule out over a period of about two weeks while gradually decreasing the dosage, the incidence of delayed filling of the breasts may be considerably reduced. If therapy is not started within forty-eight hours after delivery, the initial dose should be 25 mg. Delayed filling of the breasts may occur some two to twelve or more days later. As a rule, it is transitory and painless, while secretion is usually slight and watery.[22] In the manner just outlined, good results were secured in close to 90 per cent of our patients.

Prevention in the Nursing Mother (especially primiparas): Beginning right after delivery, 5 mg. of diethylstilbestrol is given daily for three to five days. Since actual milk secretion does not usually occur until the third or fourth day post partum, it is an excellent idea not to put the baby to breast until then, thus preventing many a cracked or fissured nipple. Adequate milk secretion will occur if the baby continues to nurse vigorously.[22]

Prevention After Weaning: After an adequate uplift breast support has been applied, the patient is given 25 mg. of diethylstilbestrol orally. The next day 10 mg. is administered, followed by 5 mg. daily for the next three days.

Relief of Painful Engorgement After Its Onset: Here a few milligrams of prevention would have been worth several kilograms of cure. After an adequate uplift breast binder is applied, 25 to 50 mg. of diethylstilbestrol is given orally. Relief may be apparent in eighteen to twenty-four hours in about 65 per cent. The next day 10 mg. is administered orally, followed by 5 mg. daily for three days. In about 25 per cent secondary filling may occur, while a watery secretion may persist for several days or even weeks. In contrast, when 10 to 25 mg. of testosterone propionate is given by injection, or 100 mg. of methyl testosterone is given orally, relief is usually apparent in two to twelve hours in close to 90 per cent, while secondary filling is rarely, if ever, noted.[25]

5. *Secondary Amenorrhea.*—After establishing a working diagnosis of functional amenorrhea, one should secure a complete blood count, a urinalysis, the basal metabolic rate and an endometrial biopsy. An adequate and properly cooked diet is prescribed together with desiccated thyroid. A thorough endometrial suction biopsy, performed regularly every four to five weeks, serves as a stimulative as well as a diagnostic measure.

If, after three to six or more months, the menses have not returned, a frank talk with the patient is in order. It must be emphasized that lack of menses does not make her one whit less a normal woman nor does it signify that she has become a sexless creature. If the mental maladjustment to the amenorrhea is still not corrected, diethylstilbestrol may be administered. (It should be noted that this may constitute just as real a symptom complex as hot flushes in the climacteric.) Many dose schedules have been recommended,[26] but this is the one we have found most satisfactory: Starting with 0.25 to 0.5 mg. daily, the dose is gradually raised every five to seven days until 1 mg. has been given daily by mouth for twenty-one days. Bleeding may occur in five to fifteen days. If not, 2 mg. daily is prescribed for three weeks. With each cycle of therapy the dose may be raised by 1 or 2 mg. until withdrawal bleeding does occur. After bleeding has resulted three times, the patient is given a rest for three months to note whether any improvement has occurred. If not, the patient is usually quite ready to listen to common sense and adjust herself to her amenorrhea.

6. *Primary Amenorrhea.*—Complete evaluation of the patient and the contributing factors leading to the absence of menstruation determine the course of therapy. The principal indication for the utilization of the gynecogenic activity of diethylstilbestrol is as an aid to offset the physical and psychic maladjustments that may occur.[27]

If the syndrome is functional in origin, a well balanced, properly cooked diet combined with the judicious use of thyroid over the space of many months is of prime importance. Cyclic administration of diethylstilbestrol as described may be used to accelerate the development of the secondary sexual characteristics. Since each patient presents problems peculiar to herself, therapy has to be individualized. In certain instances in which infantilism is pronounced, therapy may include the subcutaneous injection of a 10 mg. pellet of crystalline diethylstilbestrol at two or three month intervals.[28] Rest periods from therapy of a month or so is advisable at regular intervals.

GROUP 2. CONDITIONS IN WHICH ADJUNCTIVE THERAPY WITH DIETHYLSTILBESTROL HAS BEEN SUGGESTED BUT THE RESULTS HAVE SHOWN DIETHYLSTILBESTROL TO BE OF LIMITED OR NO VALUE

1. *Induction of Early Abortion.*—In 24 cases of early pregnancy in which menstruation was from one to ten weeks "overdue" and in all of which the Friedman test was positive, diethylstilbestrol was completely ineffectual in interrupting the pregnancy.[29] The daily oral dose ranged from 5 to 100 mg. for a total dosage of 50 to 500 mg. Similarly negative results have been reported with massive doses of estradiol.[30]

24. Stewart, H. L., and Pratt, J. P.: Inhibition of Lactation, Am. J. Obst. & Gynec. **41**: 555-566 (April) 1941. Abarbanel and Goodfriend.[22]

25. Abarbanel, A. R.: Treatment of After Pains and Painful Engorgement in the Puerperium with Testosterone Propionate, Am. J. Obst. & Gynec. **38**: 1043-1045 (Dec.) 1939; The Effects of Testosterone Propionate, Methyl Testosterone, Anhydro-Oxy-Progesterone and Progesterone on Lactation in the Nursing Human Being, ibid. **42**: 110-114 (July) 1941. Stewart and Pratt.[24]

26. Mazer, Israel and Ravetz.[18] Karnaky.[21]

27. Davis, M. E., and Boynton, M. W.: Indications, Clinical Use and Toxicity of 4-4' Dihydroxy-Diethyl Stilbene, J. Clin. Endocrinol. **1**: 339-345 (April) 1941.

28. The technic is given by Abarbanel and Klein.[18]

29. Abarbanel, A. R.: The Priming Action of Stilbestrol on the Gravid Human Uterus, Surg., Gynec. & Obst. **73**: 257-262 (Aug.) 1941.

30. Jeffcoate, T. N. A.: Missed Abortion and Missed Labor, Lancet **1**: 1045-1048 (June 8) 1940.

2. *Inhibition of Lactation and Suppression of Established Milk Secretion.*—Diethylstilbestrol will not inhibit the normal onset of lactation, although it will delay the appearance of the normal average amount of milk secretion until two to seven days after the drug is stopped, provided the baby continues to nurse.[22] Once lactation is established, however, as much as 500 mg. of diethylstilbestrol will not materially affect the amount of milk secretion.[24]

Several reports have appeared claiming inhibition and suppression of lactation in the human being by means of diethylstilbestrol, testosterone and other steroids. Unfortunately, these investigators have not clearly differentiated the syndrome of painful engorgement from the process of lactation. Furthermore, they have failed to evaluate properly the fact that the baby was removed from the breast, a procedure which, by itself, will suppress lactation.[23]

3. *Galactorrhoea.*—Although some investigators have reported that diethylstilbestrol will alleviate this condition, we have not been successful in a single case in a series of 6. Similar observations have been noted by others.[31]

GROUP 3. CONDITIONS IN WHICH THE ADJUVANT USE OF DIETHYLSTILBESTROL HAS SHOWN PROMISE IN PRELIMINARY CLINICAL TRIALS

1. The adjuvant use of diethylstilbestrol in the management of the induction of labor is based on its sensitizing or priming action on the uterine muscle to the subsequent action of potent oxytocics. The usual indication is a toxemia of pregnancy that is not responding to conservative treatment. The patient is given 150 to 200 mg. of oral diethylstilbestrol in divided doses, usually 15 to 20 mg. in ten hourly doses. The next morning the patient receives a medical induction followed by small doses of a potent solution of posterior pituitary. The details have been described elsewhere.[29] Diethylstilbestrol alone is ineffectual; it must be followed by a potent oxytocic in order that labor may ensue.[29] Regardless of the type of induction used, it is felt that the preliminary priming of the uterus with diethylstilbestrol helps to insure a successful outcome. Of 16 carefully chosen cases, 12 were successful, including 7 in which a previous medical induction followed by potent oxytocics had been unsuccessful.

2. In missed abortion or missed labor the fetus dies but fails to be expelled. In the majority of cases the estrogen level becomes low or disappears.[30] By priming the myometrium with diethylstilbestrol, the uterine muscle becomes sensitized to the subsequent action of oxytocics. The management of missed abortion or labor is the same as that outlined for the induction of labor.[29]

3. Uterine inertia may result from myometrial dystonia. Uterine contractions are ineffectual.

Supportive measures must be fully adequate after the diagnosis has been established. Oral diethylstilbestrol in doses of 25 to 50 mg. at one or two hour intervals for four to six doses may yield a successful result in about two thirds of the cases.[29] If labor ceases, the procedure outlined for the induction of labor may be used. Excellent responses were noted in 7 out of 10 carefully chosen patients.

4. Adjunctive therapy with diethylstilbestrol in the prophylaxis of postpartum and postabortal infections appears to offer great promise in the light of the published reports[32] and our own limited experience.

In addition to the indicated supportive measures, where infection seems most likely to ensue, such as after a criminal abortion or a difficult operative delivery from below, 5 mg. of oral diethylstilbestrol is given twice on the day of delivery, then once daily for five to ten days. If an endometritis is already present, 25 mg. is given, followed by 5 mg. daily. Oxytocics are administered daily.

GROUP 4

Diethylstilbestrol has been recommended as an aid in the management of several other conditions, but the number of available clinical reports, as well as our own experience, is insufficient for adequate evaluation. These include dysmenorrhea,[33] functional uterine bleeding,[34] nonpatent or stenosed fallopian tubes,[35] threatened abortion,[36] and prevention of pregnancy accidents in diabetes.[37] Further clinical trials are essential for the proper evaluation of adjuvant therapy with diethylstilbestrol in these conditions.

In primary dysmenorrhea, diethylstilbestrol has been recommended for such reasons as inhibition of ovulation on the one hand and stimulation of a hypofunctioning corpus luteum on the other.[33] In our experience, clinical trials with diethylstilbestrol have been very disappointing. Out of 21 cases, complete relief was achieved in 2 and partial relief in 5. In all 7, however, it was only temporary. In addition, in 3 of the remainder premenstrual breast pain was definitely accentuated, while in 2 others premenstrual irritability was definitely aggravated. One of our patients became pregnant during treatment. It turned out to be an ectopic pregnancy. The available clinical reports are too scanty for evaluation.

In the prevention of pregnancy accidents in diabetic patients the value of diethylstilbestrol is still not settled.[37] In treated cases White claims a salvage of 90 per cent of the babies compared to 35 per cent in untreated cases.[38]

SIDE REACTIONS

Review of the early clinical reports on the incidence of side reactions to diethylstilbestrol revealed a great disparity.[39] Careful studies since then, however, have served to clarify the situation. The consensus is that, when diethylstilbestrol is compared on a potency basis or even on a weight basis with estradiol or estrone,

31. Greenblatt, R. B.: Report of an Unusual Case of Lactation with Notes on Its Suppression, Bull. Univ. Hosp. Augusta, Georgia **2:** 1-16 (July) 1940. Geschickter, C. F.: Personal communication to the authors.

32. Connally, H. F., Jr.; Dann, D. I.; Reese, J. M., and Douglass, L. H.: A Clinical Study of the Effects of Stilbestrol on Puerperal Women, Am. J. Obst. & Gynec. **40:** 445-448 (Sept.) 1940. Reiss, W.: The Effects of Stilbestrol on Postabortal and Postpartum Endometritis, Zentralbl. f. Gynäk. **64:** 1921-1929 (Nov. 9) 1940.

33. Sturgis, S. H., and Albright, Fuller: The Mechanism of Estrin Therapy in the Relief of Dysmenorrhea, Endocrinology **26:** 68-72 (Jan.) 1940. Westman, A.: Maintenance of the Corpus Luteum Function in Women by Estrogenic Substances, Endocrinology **26:** 774-778 (May) 1940.

34. Karnaky, K. J.: Cause of Menstruation and Uterine Bleeding, South. M. J. **33:** 1285-1290 (Dec.) 1940. Palmer.[36]

35. White, M. M.: The Effect of Follicular Hormone on Nonpatent Fallopian Tubes, Brit. M. J. **1:** 342-344 (March 2) 1940.

36. Palmer, Axel: Clinical Experiments with Diethylstilbestrol: II. The Treatment of Uterine Bleeding, Am. J. Obst. & Gynec. **41:** 1018-1021 (June) 1941.

37. White, Priscilla, and Hunt, Hazel: Prediction and Prevention of Pregnancy Accidents in Diabetes, J. A. M. A. **115:** 2039-2040 (Dec. 14) 1940. Hurwitz, David: Pregnancy Accidents in Diabetes, ibid. **116:** 645 (Feb. 15) 1941. White, Priscilla, and Joslin, E. P.: Reply to Hurwitz, ibid. **116:** 645 (Feb. 15) 1941.

38. White, Priscilla: Personal communication to the authors.

39. von Haam, Emmerich; Hammel, M. A.; Rardin, T. E., and Schoene, R. H.: Clinical Studies on Stilbestrol, J. A. M. A. **115:** 2266-2271 (Dec. 28) 1940. Morrell, J. A.: Stilbestrol: Summary of Some Clinical Reports on Stilbestrol. J. Clin. Endocrinol. **1:** 419 (May) 1941.

the toxic effects are similar in the experimental animal.[40] Detailed systematic studies in the human being have failed to reveal any true toxicity.[41]

Clinically, the most common side reaction encountered is nausea, especially with menopausal patients. Careful study of these patients has brought to light several important factors, each of which must be carefully evaluated. The dose level is of prime importance (table 2). A few years ago it was reported from this clinic that the higher the dosage the greater was the incidence of side reactions.[16] This has been amply confirmed.[42] Moreover, it has been found that in evaluating the incidence of side reactions the relative estrogenic potency of the substance in question must also be taken into consideration.[43]

Equally important in evaluating nausea is the patient herself.[44] Analysis of the latter reveals that two broad groups are recognizable. The first group is composed of patients in whom nausea may be considered as being incidental in nature. It includes those who are unable to take any type of oral medication including placebos, as well as those who become nauseated only when simultaneously receiving some other medication which by itself could produce nausea, such as intravenous neoarsphenamine, digitalis or ferric ammonium citrate.

TABLE 2.—*Relationship of Daily Oral Dose of Diethylstilbestrol to Incidence of True Gastrointestinal Side Reactions in Climacteric Patients: The Higher the Dose Level the Greater the Incidence of Nausea*

Dose (Mg.)	Nausea (Per Cent on Dose)
0.10	1.3
0.25	3.4
0.50	5.3
1.0	12.9
5.0	41.7

This group also embraces those patients who become nauseous with their flushes, for not infrequently the flushes may be accentuated at the start of treatment, thus aggravating the nausea. The nausea disappears as the flushes are relieved. These women are particularly liable to be nauseous on arising, a sort of "morning sickness" of the climacteric.

The second group comprises those patients in whom the nausea may be considered as a true side reaction. In this group the incidence of nausea is clearly related to the dose level (table 2). Further study disclosed that patients with a previous past history of sensitivity to fried and fatty foods are much more prone to develop nausea at a given dose level than those with a previously negative gastrointestinal history. This was shown to be statistically significant.[44]

Just why patients with a suggestive "gallbladder syndrome" are so much more likely to develop nausea when receiving diethylstilbestrol or estradiol remains to be clarified. It has been reported that estrogen may bring about a delay in the emptying time of the gallbladder.[45] Such an effect, if confirmed in the human being, would serve to explain the increased nausea in the "gallbladder syndrome" patients, for they would tend to be more sensitive.

The management of these patients should include administration of cholagogues. Two teaspoons of magnesium sulfate once or twice a day are usually effective without causing cramping or diarrhea. Mild mercurous chloride, crude bile salts or purified bile acids may also be used. The nausea experienced by patients with a previously negative gastrointestinal history does not usually present much difficulty. Its incidence may be considerably reduced by starting with a small dose level, 0.1 to 0.25 mg., and then raising it gradually if necessary. Administration of cholagogues is also helpful. With the majority of these patients the nausea is usually transient, disappearing in spite of continued treatment.

A word should be said about dosage. One mg. of oral diethylstilbestrol daily is approximately equivalent to injecting either 1 mg. of estrone (theelin) daily or 1 mg. of estradiol benzoate about every third day. Clearly, then, a daily dose of 1 mg. is a relatively large dose, especially when it is recalled that, in contrast to estradiol and estrone, stilbestrol is not inactivated by the liver.[2] Consequently a much higher amount of active estrogenic substance is available to the body. Furthermore, it takes from three to as much as twelve days for the human being to excrete a given dose of diethylstilbestrol in contrast to the two or three days required for estradiol and estrone.[46] In short, a cumulative effect occurs, so that even 0.1 mg. daily of oral diethylstilbestrol is not such a small dose after all.

Regarding the possible carcinogenic action of diethylstilbestrol in the human being, the discussion can best be summarized as follows: According to Geschickter, the mammary cancers induced in rats by injection of estrogenic substances are due to the physiologic changes produced rather than to the carcinogenic nature of the chemical used.[47] Further, Novak,[15] in presenting the clinical phase of the problem, succinctly concluded that "it would . . . be carrying conservation to an extreme to deprive the menopausal patient of proper estrogen therapy . . . merely on the basis of this slight theoretical possibility."

SUMMARY AND CONCLUSIONS

Diethystilbestrol, a nonsteroidal chemical substance, is actually a constitutional drug, possessing, among other properties, potent gynecogenic activity. The latter attribute, plus the fact that diethylstilbestrol is therapeutically efficacious orally as well as inexpensive, is the cause of its widespread use in the management of certain gynecic conditions.

Diethylstilbestrol, being but a single drug, can logically comprise just one adjunctive part of a rational therapeutic regimen. The latter, in order to be ade-

40. Castrodale, Dante; Bierbaum, Olga; Helwig, E. B., and MacBryde, C. M.: Comparative Studies of the Effects of Estradiol and Stilbestrol on the Blood, Liver and Bone Marrow, Endocrinology **29**: 363-372 (Sept.) 1941. Page, R. C.; Russell, H. K.; Schwabe, E. L.; Matthews, C. S., and Emery, F. E.: Chronic Toxicity Studies of Diethylstilbestrol, Endocrinology **29**: 230-239 (Aug.) 1941.

41. Freed, S. C.; Rosenbaum, E. E., and Soskin, Samuel: Alleged Hepatotoxic Action of Stilbestrol, J. A. M. A. **115**: 2264-2266 (Dec. 28) 1940. MacBryde, C. M.; Freedman, Harold; Loeffel, Ellen, and Castrodale, Dante: The Synthetic Estrogen Stilbestrol: Clinical and Experimental Studies, ibid. **115**: 440-443 (Aug. 10) 1940. Aaron, A. H.; Meyers, Frank; Lipsitz, M. H., and Hubbard, R. S.: Toxicity Studies on Stilbestrol, Am. J. Digest Dis. **8**: 437-441 (Nov.) 1941. von Haam, Hammel, Rardin and Schoene.[39]

42. Davis, M. E.: Personal communication to the authors. Greene and Dorr.[18] Mazer, Israel and Ravetz.[18]

43. Davis.[42] Greene and Dorr.[18] Mazer, Israel and Ravetz.[18] Abarbanel.[44]

44. Abarbanel, A. R.: Clinical Evaluation of Adjunctive Therapy with Stilbestrol Monomethyl Ether with Comments on Toxicity, J. Clin. Endocrinol. **2**: 386-391 (June) 1942.

45. Smith, J. J.; Pomarane, M. M., and Ivy, A. C.: Influence of Pregnancy and Sex Hormones on Motility of Gallbladder, Am. J. Physiol. **132**: 129-140 (Feb.) 1941. von Haam, Hammel, Rardin and Schoene.[39]

46. Caffier, P., and Oezkayaalp, E. S.: Zur Frage der Ausscheidung der Stilben-Präparate, Zentralbl. f. Gynäk. **63**: 1218-1231 (June 3) 1939. Mazer, Israel and Ravetz.[18] von Haam, Hammel, Rardin and Schoene.[39]

47. Geschickter, C. F.: Mammary Carcinoma in Rat Induced by Estrogen, Science **89**: 35-37 (Jan. 13) 1939.

quate, necessitates treatment of the total patient, the sum of her mental as well as her physical ills.

In the general management of a patient with one of the following conditions, adjunctive therapy with diethylstilbestrol may be of definite value: (*a*) severe climacteric vasomotor instability, (*b*) essential senile vulvovaginitis including generalized essential senile pruritus, (*c*) juvenile vulvovaginitis, (*d*) prevention or relief of puerperal painful engorgement of the breasts and (*e*) amenorrhea, secondary or primary.

The adjuvant use of diethylstilbestrol is of no value whatever in the general management of the following conditions: (*a*) induction of early abortion, (*b*) suppression of lactation and (*c*) galactorrhea.

In the management of primary dysmenorrhea, adjunctive therapy with diethylstilbestrol is of very limited value.

Analysis of gastrointestinal side reactions to diethylstilbestrol, especially in climacteric patients, reveals the following: (*a*) The higher the dose level, the greater the incidence of nausea. (*b*) The relative estrogenic potency of the substance in question must be considered in evaluating side reactions. (*c*) Nausea may be an incidental or a true side reaction, depending on the patient. (*d*) Patients with a previous history of sensitivity to fried and fatty foods are much more prone to develop nausea at any given dose level than those with a previously negative gastrointestinal history. (*e*) The pregnant and puerperal patient, including those with a pronounced toxemia and even eclampsia, with evident cardiorenal and hepatic damage, may easily handle as much as 250 mg. of oral diethylstilbestrol a day without evident side effects.

ABSTRACT OF DISCUSSION

DR. EMIL NOVAK, Baltimore: The fact that a new hormonal chemical substance like diethylstilbestrol can produce the biologic effects formerly attributed only to the intrinsic vital principles which we recognize as hormones must have been startling to many, but it has been established beyond a doubt. If there is any criticism of this paper it is that, for the sake of completeness, the authors have included a discussion of many indications for the use of the drug which are of questionable value. Those of importance are those included in table 1, embracing especially menopausal symptoms, the gonorrheal vulvovaginitis of children and senile vaginitis. The authors properly stress the inadequacies of diethylstilbestrol in the treatment of amenorrhea, while many of us may feel that the problem of painful engorgement of the breasts is not as frequently important as their discussion might indicate and that very simple measures will often make patients comfortable. After a number of years of clinical and laboratory study it seems definitely established that the unpleasant toxic effects discussed in the paper are never of serious import to the patient. Moreover, when the dosage is very conservative the incidence of these side effects is probably not over 10 per cent, and certainly nothing like the 80 per cent which some authors have reported in the past. By far the most frequent indication for diethylstilbestrol is in the treatment of menopausal vasomotor symptoms when these are troublesome enough to call for direct treatment. In my judgment diethylstilbestrol has been a genuine boon for this indication, making unnecessary in most cases the long continued and expensive hypodermic medication on which we formerly relied. We have all seen "estrogen addicts" created by the automatic resort to "shots" at stated intervals regardless of whether or not the symptoms justify any medication. For similar reasons no woman should be started on diethylstilbestrol therapy in any routine fashion for an indefinite period. In few indications is individualization of treatment more important than in the management of the menopause.

DR. ROBERT B. GREENBLATT, Augusta, Ga.: The authors have pointed out the clinical indications of diethylstilbestrol therapy. I agree with them in principle. There is one point with which I take issue, namely the contention that diethylstilbestrol is not of value in the suppression of lactation. In my experience diethylstilbestrol has been as effective as the gonadal steroids. Androgens and estrogens are capable of limiting the amount of lactation by preventing release of the lactogenic hormone from the hypophysis; they do not necessarily suppress it. If the sucking reflex is removed, lactation will stop by itself, and so diethylstilbestrol may be used temporarily to limit milk production while the nursing infant is taken away from the mother's breast. One indication for diethylstilbestrol worth stressing is its use in dysmenorrhea. Steroid hormones are expensive and the average patient cannot afford the use of such hormones as estradiol benzoate and testosterone propionate. In selected cases diethylstilbestrol in vaginal suppository form in 0.2 to 0.5 mg. dosage may be administered vaginally during the intermenstruum, and the dysmenorrhea will be alleviated in about 60 per cent of the cycles. Since diethylstilbestrol is relatively cheap, it is a boon to those who cannot afford expensive therapy. Toxic reactions are frequently observed with the oral doses formerly advocated. However, when other forms of medication are used, effective results may be obtained with minimal side reactions. The percutaneous use of diethylstilbestrol in an alcohol vehicle, diethylstilbestrol dissolved in alcohol for oral use, or particularly diethylstilbestrol employed vaginally as a suppository constitute effective methods which have a low incidence of toxic or side reactions. Perhaps nausea and vomiting are not entirely simple phenomena due to the action of the drug on the central nervous system. A contributing factor when oral medication is used may be the local action on the gastric mucosa. I found that, when vaginal suppositories were employed, some patients complained of nausea, and in addition there was vaginal soreness, indicating that the action of the drug locally was somewhat irritating. I do not feel that diethylstilbestrol is toxic in physiologic doses. Kreitmair showed that the daily administration of 1 mg. per gram of body weight would kill a mouse in ten days' time, but such comparatively massive doses do not constitute a priori arguments against the use of diethylstilbestrol in clinical practice. Proper dosage, and not overdosage, is the essential answer to the argument.

DR. JOSEPH A. HEPP, Pittsburgh: I have treated 343 women with diethylstilbestrol, and toxic symptoms were noted in 6.12 per cent of these patients. Early in the use of diethylstilbestrol with menopausal patients, toxic symptoms were frequently encountered. I believe I tried to obtain results too quickly. Now it seems that one can secure results with a much smaller dose. Diligence to observe overtreatment should be practiced. During an observation of thirty-four months there have been no harmful effects from the use of diethylstilbestrol. The production of uterine bleeding in postmenopausal women has frequently been mentioned by investigators in the field of estrogenic therapy. This is usually due to too much medication over a prolonged period of time. There is excessive estrogen stimulation of the endometrium. Needless to say, this bleeding is a most distressing symptom to a woman who has stopped menstruating many months or even years previously. The medication should be discontinued when this type of bleeding is encountered, and the dosage should be decreased if treatment is resumed. In our group there have been a number of patients in whom there was no effect on the systolic and diastolic blood pressure, even though definite improvement was noted in the hot flushes. This absence of effect on the hypertension was observed in the physiologic menopause group as well as the induced menopause patients.

DR. CARLOS A. P. LAMAR, Miami, Fla.: My experience with diethylstilbestrol for nearly three years agrees closely with that described here today. It should be stressed that, for the treatment of the climacteric, very small doses should be employed. There is no need to increase the dosage to the point of producing endometrial stimulation. In cases of senile vaginitis in which larger doses may have to be tried in an attempt to produce relief and endometrial stimulation and bleeding is produced, I have found that the effect can be neutralized by the concomitant

administration of oral synthetic progesterone substances. I do not quite agree with the authors' conclusions regarding the suppression of lactation with diethylstilbestrol. I find that diethylstilbestrol administered to the postpartum woman in doses of 5 mg. four times a day for from four to six days suppresses lactation without the need for binders. Regarding the toxicity of diethylstilbestrol by the several routes of administration, I have found several striking facts. Certain patients will have excessive toxicity by mouth while tolerating extremely large doses parenterally.

DR. KARL JOHN KARNAKY, Houston, Texas: I want to stress that the most important thing is that by giving 1 mg. daily of diethylstilbestrol to the menopausal woman or any woman who still has her uterus you will produce bleeding; therefore I advocate smaller doses. The authors mentioned dysfunctional uterine bleeding. I have had more than 800 patients during the last five years. I give such a patient from 5 to 25 mg. of diethylstilbestrol into the anterior wall of the cervix. I have now given more than four thousand injections into the anterior wall of the cervix without any harm whatever. For twenty consecutive nights I give a 5 mg. diethylstilbestrol tablet. Two to eight days after the last tablet, she will spot for two or three days, bleed for two or three days and then spot again for two or three days. If she bleeds excessively give one half of a 5 mg. diethylstilbestrol tablet every hour until the bleeding is checked. Within fourteen to twenty-one days, 87 per cent of the patients had a premenstrual endometrium on subsequent examination. As a result of experience with diethylstilbestrol in the treatment of dysfunctional uterine bleeding I feel that radium or a hysterectomy is seldom indicated. I do not find curettage necessary for therapeutic purposes. In threatened abortions I give five 5 mg. (25 mg.) diethylstilbestrol tablets every fifteen minutes until the pain and bleeding stop, then two 5 mg. tablets every hour for six doses, then one 5 mg. tablet every hour for six doses and then 10 mg. every night until the eighth month. As to the modus operandi of diethylstilbestrol in these conditions one must for the present resort chiefly to conjecture. The dosage determines the effect. Small amounts produce proliferation of the endometrium and large doses inhibit the pituitary oxytoxins on the uterine musculature, regulate the endometrial vascular system by keeping the spiral arteries dilated and stimulate natural progesterone production, which helps to complete the changes in the endometrium, which I think is one of the most important functions of the progesterone. They also inhibit the excess production of gonadotropin of the anterior pituitary, cause normal rhythmic contractions of the uterus and aid in the normal metabolism of progesterone and estrogens to estrone and estriol. I believe that diethylstilbestrol will replace corpus luteum for the treatment of threatened and habitual abortions and premature labor.

DR. JOHN M. FREIHEIT, Waterbury, Conn.: Initially I have done a pretty good job with the natural hormones. The effect of the natural hormones on the side effects of the menopause and the various functional disorders is very good. Then along came this very strong, potent synthetic hormone, which was put out without a great deal of preparation and used rather indiscriminately. The effects of the natural hormone were immediately exacerbated by the very strong synthetic hormone, not only by serious side effects as nausea and vomiting and general discomfort, but even by return of bleeding sometimes after the menopause had established itself. I don't believe that even natural hormone should be given in the menopausal state unless the pelvic organs are regressing to the natural senile state. In other words, if one takes a pelvic structure which is hypertrophying and give even the natural hormone, one has a great deal of abnormal symptomatology resulting from it. I think, therefore, that in proper cases the use of natural hormone still should supersede the giving of large doses of synthetic hormone. One should at least start patients on natural hormone when indicated instead of giving large doses of synthetic hormone indiscriminately and use the synthetic hormones in small doses to prolong the effects of the natural hormones after the desired effects have been produced.

THE DIAGNOSIS AND TREATMENT OF PRIMARY INTRATHORACIC TUMORS

FRANK S. DOLLEY, M.D.
LOS ANGELES
AND
CAPTAIN LYMAN A. BREWER III
MEDICAL CORPS, ARMY OF THE UNITED STATES

Because the incidence of primary intrathoracic tumors is apparently increasing, and because with early recognition the great majority may be cured in competent hands with radical surgery, the diagnosis and management of this great group of tumors is becoming more and more important. The literature on this subject has become voluminous and complex, the individual reports dealing mainly with one particular type of neoplasm. When confronted with the individual case, however, the clinician must consider all the possibilities. Therefore it seems important to condense into one article a review of the practical management of this entire group of tumors. Because of the limitations of space, our case reports, covering over 40 extrapulmonary intrathoracic neoplasms removed surgically, on which this review is based, cannot be included. They will be published elsewhere.

PRIMARY TUMORS OF THE LUNG

Adenomas of the bronchi exhibit a growth potential somewhere between a purely benign tumor and one of proved malignancy. There is considerable dispute in the literature just how these tumors should be classified. We are certain that the conservative point of view is to regard them as potentially malignant. When they are entirely endobronchial, which is not common, they may be safely treated by bronchoscopic removal. However, one must carefully check every case for local recurrence and extrabronchial extension. We have found the planogram of great help in demonstrating extrabronchial extension, which is an indication for pulmonary resection, either lobectomy or pneumonectomy. Pulmonary suppuration, the inevitable result of chronic obstruction caused by presence of tumor in the bronchus, may also make lobectomy or pneumonectomy imperative.

Clinically, the most prominent symptoms and signs of adenoma are those of bronchial obstruction. Atelectasis, lung abscess and bronchiectasis are the common findings. Thus it is the secondary changes in the lung fields, produced by bronchial obstruction, that are usually seen on the chest roentgenogram rather than the tumor itself. Occasionally hemoptysis may be the presenting symptom and the x-ray examination fail to reveal the cause of the hemorrhage. Bronchoscopy is diagnostic, as the great majority arise in the main bronchi. One must not be content with a single piece of tissue for biopsy, as the cell type varies. Often only a superficial inflammatory tissue is obtained, while the real tumor is present at a level just beneath the site of the biopsy. At bronchoscopy we are accustomed to remove as much tumor as possible with the biopsy forceps. The base is then well cauterized with either the electric cautery or 50 per cent silver nitrate. How-

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ever, excessive bleeding may prevent adequate bronchoscopic removal of the tumor and be a further indication for pulmonary resection. If recurrence of the tumor occurs with or without bronchial obstruction, radical pulmonary resection is certainly the procedure of choice. Adenomas of the bronchus may grow slowly and perhaps imperceptibly for years and then as the result of some unknown growth stimulus rather suddenly undergo malignant transformation. Finally, lung suppuration secondary to neoplastic bronchial obstruction is usually the immediate cause of death, whether the tumor is benign or malignant.

For these reasons we believe in most instances that radical pulmonary resection is the safest form of treatment.

2. *Malignant Pulmonary Tumors.*—The great majority of primary bronchial tumors are carcinomatous in character. At some time early in the course of their development, all bronchogenic carcinomas are confined entirely to the involved lung. A total pneumonectomy at that time would result in their complete extirpation. Many such cases well past the five year period are on record. The comparatively low operative mortality among those competent to do this work more than justifies immediate exploration in view of the fact that without extirpation death ensues. Following lung removal, it is astonishing how little the life of one who does not indulge in violent physical exertion is limited.

It is of the greatest importance, therefore, that we constantly keep in mind the early suggestive symptoms of bronchogenic neoplasms. They may be divided into two groups: (1) bronchial irritative symptoms and (2) bronchial obstructive symptoms. In the former the growth, still too small to obstruct a bronchus, irritates a vagal nerve branch; a nonproductive harassing cough results, often accompanied by wheezing, sometimes with an occasional streak of blood, more often not. If such a patient does not respond to the usual cough remedies, he should be told of the possible existence of a tumor and bronchoscopy strongly advised (regardless of the fact that he usually feels perfectly well except for the annoying cough).

Not rarely a patient states that he has had a cigaret cough for years or has had chronic bronchitis but that in recent weeks its character has changed with or without blood streaking. An early bronchogenic neoplasm may well be the cause of this change. X-ray examination of the chest often shows only increased lung markings or an irregular shadow at the hilus. Early diagnosis before metastasis has occurred can be made only with the bronchoscope.

Then there is the group in which the symptoms of bronchial obstruction are evident. The symptoms roughly fall into two classes:

1. There is sudden, acute febrile onset with chills, fever and signs of pneumonic consolidation.. The type of pneumonia, however, is an atypical one and convalescence is protracted. A tragically large number of such people are told they have delayed resolution, a term that should be discarded from our nomenclature. Bronchial obstruction from malignant neoplasm is not uncommonly the causative factor. At this stage the growth may be confined entirely to the involved lung. When an atypical pneumonia shows little tendency to clear, without delay bronchoscopy should be done

2. If pyogenic bacteria are imprisoned distal to a neoplastic bronchial obstruction, a lung abscess or pulmonary suppuration may develop. Bronchoscopy is advisable in all such cases. It is the procedure of choice in any event, since bronchial drainage from the affected area is usually more adequate thereafter.

Seventy-five per cent of these tumors can be visualized through the bronchoscope. The x-rays take up where the bronchoscopy leaves off, as the peripheral types usually cast circumscribed shadows of homogeneous density apparent on the radiolucent lung fields. However, since biopsies cannot be taken, this type is more difficult to diagnose. Needle aspiration is often followed by the development of secondary growths along the needle path and should be reserved for those cases manifestly inoperable. Careful sputum examination may show malignant cells. In many instances it is only by surgical exposure of the lung that the true identity of the growth can be determined. Too often because of this uncertainty, lung removal is postponed until extension to the mediastinum renders lung removal futile. All unexplained pulmonary masses must be considered carcinoma of the lung. If metastasis cannot be proved, exploration is indicated.

PRIMARY TUMORS OF THE MEDIASTINUM

The symptoms relative to these tumors are in a very large measure due to the pressure of the growth on contiguous structures. The degree of interference with the functions of the mediastinal organs varies with the location of the tumor, its size and the presence or absence of actual invasion of these organs. Their interpretation is seldom difficult. Pain may be dull or sharp, local or referred. Cough may be absent or extremely distressing. As a tumor grows, it may eventually occlude a bronchus with resultant symptoms of pulmonary infection from bronchial obstruction. Dyspnea, a common symptom, does not necessarily vary with the size of the tumor. A comparatively small growth may cause considerable difficulty in breathing if it obstructs the trachea or bronchus. Hoarseness, dysphagia and engorgement of veins of the neck may be present. If the neoplasm is a benign one, death is entirely the result of compression on surrounding organs.

When the neoplasm is seen by x-ray examination to lie within the mediastinum, it is desirable to consider the various kinds of tumors that are at some time during their existence amenable to surgical removal, their characteristics, their locations and their usual x-ray appearance. Thus by consideration and selection the correct preoperative diagnosis can frequently be made.

1. *Teratoid Tumors* (dermoids and teratomas).—Since most dermoid tumors of the mediastinum (even though they contain hair) are made up of cells representative of three germ layers, the term "teratoid" tumor as used by Harrington[1] is more accurate. We discuss them together, as clinically they are very similar. The "dermoids" tend to be more cystic, while the teratomas are more cellular and thus are more prone to malignant change. With few exceptions these teratoid tumors are primarily located in the anterior mediastinum from the level of the manubrium to the diaphragm. They are by far the most common benign mediastinal tumors. While they may be centrally placed and be apparent both to right and left of the mediastinal borders, as a rule they project sharply out into the lung fields with a clearcut, well defined convex border. Often trauma apparently initiates increase in size. It is probable that they are present from birth; yet it is usually during the second and third decade that progressive enlargement occurs and pressure symp-

1. Harrington, S. C.: Surgical Treatment of Intrathoracic Tumors, Arch. Surg. **19**: 1679 (Dec., part 2) 1929.

toms develop. It is unusual for these tumors to exert pressure on a bronchus sufficient to produce acute pneumonitis. They may grow to enormous size, almost completely collapsing a lung, but without obstruction to the major bronchi. Calcium is often evident in the walls of the cyst. While teeth may be present, they are not common. Hair almost always is found in the dermoids. If a dermoid ruptures into a bronchus, the presence of hair and thick cloudy fluid containing fatty material establishes the diagnosis. While sarcomatous degeneration not rarely occurs, invasion of the cyst wall is late, so that the enucleation of the tumor usually cures. Even when of huge size, they may be enucleated without great difficulty.

Shortness of breath, pain, cough—any one or all of these symptoms may be present. Of course, as in all other mediastinal tumors, other pressure manifestations may exist. The x-ray examination reveals a clearcut, anteriorly located, somewhat spherical shadow, nonpulsile on fluoroscopic examination, projecting usually into the lung fields. Needle aspiration is not advisable. Often the cyst contents are too thick to be sucked through a needle even of large caliber. In addition, it is by no means certain that even the comparatively slight hemorrhage from the trauma of such a procedure may not increase the rapidity of enlargement of a tumor already enlarging. If a small "test" dose of radiation therapy is given over the tumor, in three weeks' time any appreciable radiosensitivity may be noted.

2. *Mediastinal Lipomas and Liposarcomas.*—Mediastinal lipomas are very liable to sarcomatous change. The two types, therefore, are considered together. The symptoms and treatment are identical. The lipomas cause symptoms from pressure, while the liposarcomas are extremely invasive and may metastasize. At operation, even with the most careful painstaking dissection, bits of fatty sarcomatous tissue are likely to be left behind, resulting in recurrence.

Not only do these primary mediastinal tumors extend laterally into the lung fields, but finger-like processes often burrow along fascial planes to become palpable on the chest wall. Therefore any soft, rather movable, mass discovered either parasternally or paravertebrally beneath the deep fascia is more than likely to be but the superficial extension of a mediastinal lipoma.

There are two roentgenologic features of mediastinal lipomas that are strongly suggestive. Since the consistency of the tumor is scarcely more solid than a fibrin clot, the transmission of the cardiac impulse is so complete that under the fluoroscope these tumors usually appear to pulsate with an undulating, wavelike motion. Indeed, if their location should conform to that of the aorta and if the Wassermann reaction should be positive, the diagnosis of aneurysm would seem to be established. The other suggestive finding is that often in an examintion of the x-ray film the peripheral zone of the tumor seems thinner than its central portion.

They may grow to enormous size without giving symptoms. Eventually shortness of breath and pain develop, as well as other symptoms of pressure on neighboring organs. Prompt surgical removal is indicated, since these tumors tend to grow very rapidly when once increase in size is apparent. The danger of sarcomatous change makes their immediate excision the more desirable.

3. *Mediastinal Tumors of Neurogenic Origin.*—This group is a very complex one. The tumor under consideration may be derived from a sympathetic ganglion, the sheath of a sympathetic nerve, a spinal nerve or an intercostal nerve. The character of the tumor depends on whether it is derived from the myelin sheath, the sheath of Schwann or the connective tissue sheath. Thus a wide variety of neurogenic neoplasms may develop from the same mediastinal region; benign neurofibromas or neurogangliomas, and the malignant neuroblastomas and sympathicoblastomas, neurogenic sarcomas, and so on.

All these tumors arise in the posterior mediastinum, usually lie in the costovertebral gutter and are more often found in the upper portion of the chest than in the lower. The benign neurofibromas and gangliomas project laterally into the lung fields and on x-ray examination present clearly defined borders, convex outward. Pain locally or along the course of an involved intercostal nerve is commonly present. Occasionally a pneumonitis from obstructive pressure against a neighboring bronchus leads to the detection of the tumor. With complete bed rest permitting the neoplasm to drop away from the compressed bronchus, the pulmonary inflammation usually clears. Surgical extirpation of the tumor should then be strongly advised before more serious pulmonary obstruction develops.

Many such tumors are picked up during a routine chest examination. They have given no symptoms. While they remain asymptomatic for years, their removal is desirable if no particular contraindication exists. Certainly at regular intervals they should be checked by x-ray examination. If increase in growth becomes evident, they should be removed at once. It should be remembered that neurogangliomas are frequently directly over the vertebral bodies, centrally located in the mediastinum, and that such a location does not necessarily indicate malignancy and inoperability. Their outline is very definite and clearcut.

In the malignant group neuroblastomas and neurosarcomas, certain signs suggest their character. Erosion of ribs or of vertebral bodies is of grave import; it is seldom present in connection with benign growths. Horner's syndrome and hoarseness usually mean that the growth is malignant in character, as do dysphagia and a nonproductive, high pitched, dry, metallic cough. Radiant therapy is particularly valuable in this group of cases, both as a diagnostic and as a therapeutic measure. There is little likelihood that they are surgically removable. Yet, if x-ray treatment does not clearly reduce its size and the borders of the growth are comparatively well defined, surgical exploration is indicated. Much too frequently a tumor considered though not proved to be malignant has been found at autopsy to be benign, and death was due entirely to pressure on the surrounding organs.

It is important to bear in mind that the benign tumors of neurogenic origin occurring in or near a spinal foramen may extend into the spinal canal, compressing the cord. These so-called "hourglass tumors" are by no means rare. If not of too long standing, their excision can be successfully accomplished following removal of the overlying lamina. It must be remembered too that these neurofibromas may occur as a part of von Recklinghausen's disease. Finally, all these previously benign growths may undergo sarcomatous degeneration and are therefore always potentially malignant.

4. *Fibroma and Fibrosarcoma of the Mediastinum.*—A simple fibroma within the mediastinum producing symptoms leading to its diagnosis is rare. In almost all such growing tumors, sarcomatous change has

already taken place. The symptoms are due to compression or interference in function of the surrounding mediastinal organs. X-ray examination shows a clear-cut or spherical shadow which cannot be distinguished roentgenographically from other circumscribed tumors. Since they may originate from a vertebra or the posterior surface of the sternum, they may be located in the posterior or anterior mediastinum. Extension may occur into a spinal foramen causing cord symptoms. For some time, even with sarcomatous degeneration present, they may remain encapsulated. During this period they can be completely enucleated without particular difficulty. When extension beyond the capsular wall has occurred, invasion into and around the surrounding structures progresses very rapidly.

5. *Tumors of the Thymus.*—The most interesting group of thymic tumors is that associated with myasthenia gravis. In more than half of the patients suffering from this disease pronounced hyperplasia or neoplastic change has been found. With few exceptions the neoplasms are benign in character. Aronson [2] in 1937, Blalock [3] in 1939 and Poer [4] in 1941 successfully removed thymic tumors associated with myasthenia gravis. All symptoms of the disease disappeared following operation. Aronson's and Blalock's tumors were benign. Poer's showed evidence of carcinomatous change. We attempted to remove a malignant thymoma in an advanced case of myasthenia gravis. However, extensive infiltration into the mediastinal structures, especially the wall of the right innominate vein, prevented complete removal. (The patient died of a postoperative pneumonia.) Recently Blalock has removed the thymus in 6 cases of myasthenia gravis. In all some degree of hyperplasia was found. No report concerning this group has been made. While the dramatic results obtained in these 3 cases are encouraging, the exact relationship of thymic neoplasms or thymic hyperplasia to myasthenia gravis is as yet not clear. Roentgenologically it is difficult to distinguish between the benign and malignant thymic tumors; in all cases of myasthenia gravis with thymic tumor, exploration should be done.

Except in myasthenia gravis, benign tumors of the thymus are comparatively rare. Simple hyperplasia or persistent thymus is usually amenable to x-ray treatment. Surgical extirpation is seldom indicated, nor are malignant tumors of the thymus common. Almost without exception they are inoperable when local symptoms develop.

6. *Lymphosarcoma and Hodgkin's Disease.*—The most common tumors of the mediastinum are those of the lymphoma group. There still exists much confusion concerning the various types of malignant diseases arising in the mediastinal lymph nodes. Several exhaustive reports have appeared in the literature attempting to establish tables in differential diagnosis. Because of great variability in symptoms, laboratory findings and clinical course, uncertainty concerning the actual type of lymphatic involvement is usual. Only the microscopic examination of some accessible involved lymph node or occasionally a punch biopsy positively identifies it.

The usual symptoms of involvement or compression of mediastinal organs are present late in the course of the disease. Early the symptoms of a mild pulmonary infection predominate with dry cough, continued fever and a leukocyte count to 15,000. We have not found the differential leukocyte count helpful in making the diagnosis. Occasionally mediastinal or lung abscess is suspected and the patients are referred to the surgeon for drainage. The x-ray picture varies from a circumscribed mediastinal mass to irregular densities projecting laterally into the lung fields. Rarely isolated pulmonary masses resembling metastatic malignancy are present. In the lateral films the posterior mediastinal space usually is clouded or obliterated. It is unusual for Hodgkin's disease to remain confined entirely to the mediastinum. After a period of time, frequently the axillary or cervical nodes are involved. Biopsy obtained from one of them solves the diagnostic problem. Multiple shadows confined entirely to the mediastinum are more likely to be sarcomatous in nature.

Surgery has been able as yet to offer nothing in either condition. Fortunately, almost all of these primary lymphatic malignant growths are very radiosensitive. Total disappearance under radiant therapy is by no means rare. However, permanent cure seldom results.

7. *Primary Sarcoma of the Mediastinum.*—Primary sarcomas originating within the mediastinum are rare. The great majority represent malignant degeneration of neoplasms that were at first benign. These have already been described. Early in their development these primary sarcomas may prove removable. They can arise from any of the connective tissue elements of the mediastinum. If their location is lateral they extend out into the lung fields. At first, before invasion of surrounding structures has occurred, their boundaries are clearcut. They cannot, therefore, be distinguished from benign tumors that have been mentioned. Only their comparative rarity makes their presence unlikely.

The ideal treatment is the removal of the benign mediastinal tumor before it becomes malignant, regardless of the paucity of symptoms.

SUPERIOR PARAMEDIASTINAL OR SUPERIOR SULCUS TUMORS

Pancoast [5] first described this syndrome. It was his opinion that this type of tumor arose from branchial cleft derivatives and was a definite neoplastic entity. As additional data accumulated, however, it was discovered that various tumors in this region could give the signs and symptoms described by Pancoast.

The apex of the lung lies immediately lateral to the first thoracic vertebra, protruding upward through the first rib circle. The first thoracic nerve is in contact with the pleura, and the first and second intercostal nerves are just mesial to its apex. The sympathetic trunk with its ganglions lies just mesial to it. The phrenic and recurrent laryngeal nerves are not far distant. Thus a neoplasm arising in this region may cause manifold symptoms early in its growth.

Early extension involving first thoracic and intercostal nerves and the sympathetic chain occurs. The symptoms, therefore, are predominantly mediastinal rather than pulmonary.

Pain, sometimes becoming extreme, is uniformly present in the shoulder and extending down the upper extremity and often to the base of the head. Eventually paresis of the hand may develop. Horner's syndrome is usually present. Frequently such unfortunates are

2. Aronson, S. F.: Myasthenia Gravis: Discussion with Presentation of a Case Associated with Thymoma, Ann. Int. Med. **15**: 137 (July) 1941.

3. Blalock, Alfred: Tumors of the Thymic Region and Myasthenia Gravis, Am. J. Surg. **54**: 149 (Oct.) 1941.

4. Poer, D. H.: Effect of Removal of Malignant Thymic Tumors in a Case of Myasthenia Gravis, Ann. Surg. **115**: 586 (April) 1942.

5. Pancoast, H. K.: Superior Pulmonary Sulcus Tumor, J. A. M. A. **99**: 1391 (Oct. 22) 1932.

treated for "neuralgia" for weeks or months. X-ray examination, however, discloses a roughly triangular shadow continuous with that of the mediastinum, corresponding closely to the so-called axygos lobe area. The following differential diagnosis of abnormal shadows of probable neoplastic origin occurring paramediastinally in this upper thoracic quadrant is of importance both from a diagnostic and from a therapeutic standpoint.

1. *Bronchogenic Carcinoma, Main Bronchus Upper Lobe.*—A wide triangular shadow with its apex at the pulmonary hilus and its base above extends outward from the upper mediastinum to fill in completely the circle of the first rib. Such a shadow usually represents an atelectatic upper pulmonary lobe. A bronchogenic neoplasm obstructing the main bronchus is commonly the cause. Shoulder girdle pain and Horner's syndrome usually are absent. Cough with or without production usually, but not always, is a symptom of prominence. Bronchoscopy may reveal the neoplasm. Because scarcely more than the orifice of the upper lobe bronchus can be seen, often the growth within the bronchus cannot be visualized even with the use of a 45 degree angle mirror placed in the bronchoscope to look up the branch bronchus. If such symptoms occur in conjunction with such a shadow in a person in the cancer age, neoplastic obstruction must be considered the probable causative factor. We have recently tried implantation of radium in inoperable carcinoma in a manner similar to that to be described for sarcoma. No improvement was noted. Prompt surgical exploration is the procedure of choice. Early in its course, lung removal may prove curative.

2. *Bronchogenic Carcinoma, Branch Bronchus Upper Lobe.*—Occasionally a smaller shadow similar to the one described appears in this region with its base just above the hilus. Instead of involving the entire apical region with a homogeneous shadow it usually is comparatively small, with less definite borders. This shadow represents lobular atelectasis resulting from an obstructing carcinoma of a branch bronchus of the upper lobe near the mediastinum. There are no nerve pressure symptoms as a rule and often but little cough. Bronchoscopy does not demonstrate the tumor. The diagnosis is rarely made early enough to permit surgical removal.

3. *Bronchogenic Carcinoma, Peripheral Upper Lobe Along the Mediastinum.*—A narrow triangular shadow may arise in the circle of the first rib with its base along the mediastinum. The apex does not extend to the hilus. The borders are indistinct because of fine processes extending out into the upper lobe lung field. This represents a bronchogenic carcinoma arising in the periphery of the upper lobe without producing a cough. The x-ray appearance represents the growth of the tumor itself. Because of few symptoms early in its course, as in the previous type just described, rarely can the diagnosis be made soon enough to allow surgical removal.

4. *Extrapulmonary Upper Mediastinal Tumor.*—The fourth type of superior sulcus tumor is of mediastinal origin. There is the clearcut spherical shadow in the anterior or posterior mediastinum, projecting laterally into the lung fields in the apical region. Intercostal and even shoulder pain may be present. Indeed, it is usually the patient's chief complaint. The shadow may be small, but it is unlikely that it will be triangular. The lateral bulge and convexity strongly suggest that one is confronted with any one of the mediastinal tumors previously described. Moreover, the pulmonary symptoms are slight, while Horner's syndrome, and pain extending down the arm, are rare. Posteriorly these tumors are usually neurogenic in origin, anteriorly either dermoids or teratomas. Frequently they can be enucleated without great difficulty. It must be remembered, however, that fibrosarcomas may also occur in this region.

Finally, an extrapulmonary upper mediastinal tumor may be of such soft consistency that the intrapulmonary pressure of the lung immediately lateral to it will mold it to a triangular shape entirely consistent roentgenologically with an atelectatic upper lobe; for example, lipoma, fibromyxoma, ganglioneuroma. Recently we exposed and successfully removed a ganglioneuroma following a preoperative diagnosis of probable carcinomatous obstruction of an upper lobe. The tumor was very soft and as it was released from the pressure of the contiguous lung at once assumed a roughly globular shape.

We exposed by a posterior approach another tumor corresponding in configuration and symptoms to those enumerated; that is, severe pain in shoulder and arm, Horner's syndrome. Erosion of the second rib, often noticed in these cases, was evident in the x-ray films. Biopsy at operation showed the growth to be a fibromyxosarcoma. It was invasive in character and not operable. However, radon seeds on hand for that purpose were needled into it. They were so inserted as to provide a range of radiant activity of approximately 1.5 cm. The postoperative course was a most stormy one because of an almost lethal dose of radium. The wound broke down completely, yet eventually it healed. All symptoms, including pain, which had been very severe, disappeared. For nearly two years the patient remained well. Local recurrence then appeared and death followed within a few months. His severe pain, however, did not recur. It is well to bear in mind, therefore, that definite relief may be obtained in this manner and that the possibility exists on occasion that the neoplasm may prove to be benign and removable. All attempts at extirpation of fibrosarcomas at this stage have done more harm than good.

PRIMARY TUMORS OF THE THORACIC CAGE

Primary tumors of the thoracic cage make themselves manifest by pain or the presence of a palpable mass, or both. Pain is the most important symptom. It is the result of involvement or pressure on an intercostal nerve by the tumor and so the pain can be located anywhere in the sensory distribution of this nerve. In the case of the upper three thoracic nerves the pain may be "referred" through the same segment of the cord to the brachial plexus and result in the sensation of pain in the arm. Therefore it is of great diagnostic importance to consider any thoracic, upper abdominal or upper extremity pain without a clearly apparent cause to be due possibly to a remotely located neoplasm in or contiguous to the chest wall. A diagnosis of neuralgia, whether the pain is located in the chest wall, abdomen or upper extremity, should never be made until careful x-ray examination reveals no evidence of thoracic neoplasm. This is a point of great importance too frequently forgotten and overlooked by the physician until tumor growth is so far advanced that the chance of successful surgical care has passed. Artificial pneumothorax helps to distinguish the chest wall neoplasms from mediastinal and intrapulmonary tumors.

1. *Bone and Cartilage Tumors* (Osteoma, Osteochondroma, Osteochondrosarcoma, Chondrosarcoma).—All these neoplasms may well be considered together. All such tumors are potentially malignant and should be extirpated as soon as discovered. Primarily they are benign. Even when sarcomatous change has occurred, invasion beyond the capsule is at first relatively slow. Their removal at this stage is not difficult. If invasion of the capsular wall is apparent, however, both the parietal pleura immediately surrounding them and that portion of the bony wall to which they are adherent and from which they originate must be excised together with the intervening soft tissues. Serous or even bloody pleural fluid may be present, although it is unusual. Often these tumors are not discovered under the fluoroscope. They may cast but a thin hazy shadow, and bony structures behind or in front may conceal them. Frequently it is necessary to have both a posteroanterior and an oblique Potter Bucky film in order to reveal their exact location.

Unfortunately even highly malignant tumors of the chest wall cannot be distinguished in their roentgenologic contour from benign ones. Rarefaction of adjoining ribs is highly suggestive evidence of their true character, however. Loss of weight without other apparent cause, and bloody pleural effusion, add to the gravity of the situation. If considerable loss of weight has occurred or if actual metastases are discovered or strongly suspected, the removal of the primary growth is of course contraindicated. Otherwise wide extirpation of the tumor is advisable. X-ray treatment has proved of only temporary benefit.

2. *Fibroma.*—A pure fibroma of the chest wall is rare. We have had 1 such case. A tumor roughly ovoid, 15 by 12 inches, closely embraced the ninth, tenth and eleventh ribs anterolaterally. Numerous finger-like, grayish white processes extended into muscle tissues and fascia. It seemed identical in type and in extension characteristics with the so-called desmoid that is occasionally discovered in the rectus sheath and muscle. The probability of recurrence in this type of tumor is considerable, since it is not unlikely that one or more of these long advancing tentacles may be entirely overlooked following an apparently complete and certainly painstaking dissection. Since x-ray treatment has no effect, an attempt to extirpate them surgically should be made. Recurrences, however, are to be expected and, since they represent a local growth, should be removed.

3. *Fibrosarcoma.*—These tumors are not uncommon. When pain develops leading to their discovery they have become in the great majority of cases invasive. The prognosis for complete removal is bad, although it should be attempted if no evidence of metastasis exists. X-ray treatment has little influence on their course. They usually metastasize early; therefore, not infrequently even when apparently cleanly removed, a fatal outcome is not averted.

4. *Benign Giant Cell Tumors.*—These growths are comparatively rare. Early their complete extirpation is possible. They are prone to sarcomatous degeneration. When definite evidence of growth increase exists, it is probable that metastasis has already occurred. X-ray treatment has proved of very great value in this type of neoplasm.

5. *Osteogenic Sarcoma.*—In primary osteogenic sarcoma bone destruction occurs very early. The prognosis is thoroughly bad. X-ray treatment frequently is of considerable help. Provided the extent of the growth or the presence of metastasis is not present as a valid contraindication, extirpation of the tumor with all of the immediately surrounding structures is the procedure of choice.

Ewing's sarcoma, with few exceptions, eventually proves fatal. Uniformly it occurs in persons under 30 years of age. Bone destruction is present. Metastases occur very early. Few survive, even when the primary growth is removed widely and early. Radiant therapy is often of great benefit temporarily.

SUMMARY

Having taken a bird's eye view of this great group of intrathoracic neoplasms, we are now in a position to summarize the practical points concerning each of the main types.

Primary tumors of the lung of clinical importance consist of bronchial adenomas (10 per cent) and bronchogenic carcinomas (90 per cent). The signs and symptoms of the two types are somewhat similar. Those of the adenomas may extend over a period of years while those of the carcinomas are present only for a matter of weeks or months before metastasis occurs. The symptoms are mainly bronchial irritative and bronchial obstructive. The bronchial irritative symptoms are cough, or change in character of a long standing cough with or without expectoration; perhaps blood spitting. The bronchial obstructive symptoms begin with wheezing, followed by an atypical pneumonia with protracted convalescence or lung abscess.

Bronchiectasis, a finding common with chronic bronchial obstruction, is frequently seen in adenoma of the bronchus but rarely in carcinoma. It should be emphasized that pain is a late symptom of carcinoma of the bronchus. The diagnosis can be made in 75 per cent of the cases by bronchoscopy, as this percentage of tumors arises in portions of the bronchus visible with the bronchoscope. A positive biopsy can thus be obtained. The peripheral type of bronchogenic carcinoma, invisible to the bronchoscopist, casts a shadow visible on the radiolucent lung fields which represents tumor or pneumonitis distal to secondary branch bronchial obstruction. Thus the x-rays take up where the bronchoscopist leaves off. Lobectomy or pneumonectomy will be eventually indicated in cases of bronchial adenoma because of recurrence following bronchoscopic removal, hemorrhage, extrabronchial extension or chronic pulmonary suppuration. Pneumonectomy should always be performed unless the tumor is limited to distant periphery of a lobe, when the diagnosis of bronchogenic carcinoma is made, and no metastases can be demonstrated, provided no other contraindication exists.

The death rate from intrapulmonary neoplasms (predominantly bronchogenic carcinoma) will be decreased by surgical removal only with early diagnosis. Immediate and serious attention to the following two factors is therefore imperative: 1. Prompt bronchoscopy in all cases of protracted cough, expectoration and hemoptysis, regardless of an innocent appearing chest roentgenogram and apparent excellent general condition of the patient. 2. Prompt surgical exploration in all cases of solitary enlarging pulmonary shadows not otherwise explained, especially if they are circumscribed. An occasional metastatic tumor will be removed and very rarely an inflammatory lesion. But in the vast majority of cases this early surgical exploration will save the life of many a patient with bronchogenic carcinoma.

Primary tumors of the mediastinum make themselves known by pressure on the mediastinal organs. Thus dyspnea, pain in either the chest or the arm, cough, wheezing, dysphagia, hoarseness or distention of the neck veins may be present. Neuralgia in shoulder or arm is always suggestive. X-ray examination uniformly shows a mass in either the anterior or the posterior mediastinum. Dermoids and teratomas are the most common benign tumors of the anterior mediastinum. They are circumscribed, slow growing, radioresistant tumors usually presenting symptoms in the first and second decades of life. The most common benign tumor of the posterior mediastinum is neurogenic in origin. Pain is the most prominent early symptom, while the symptoms of mediastinal obstruction come on late. On x-ray examination a round circumscribed shadow is seen in the posterior mediastinum.

The lymphosarcomas are the most common malignant mediastinal tumors. They present rapidly enlarging irregular x-ray shadows extending from either the posterior or the anterior mediastinum. Their extreme radiosensitivity distinguishes them from the benign tumors, which are radioresistant. Since lymphosarcomas are inoperable as soon as they produce symptoms, a "test dose" of x-ray therapy should be tried preoperatively in all cases of mediastinum tumor where a lymphoblastoma is a possibility. All benign mediastinal tumors should be removed surgically as soon as they are diagnosed unless a definite contraindication exists, since they may eventually prove fatal from mediastinal obstruction due to their size or because of malignant degeneration. The operative mortality in experienced hands is very low. Other less common mediastinal tumors, because of their diverse characteristics, cannot be summarized here.

Superior sulcus tumors represent a variety of new growths arising in the superior paramediastinal region. Pain in the shoulder and arm, Horner's syndrome and a dry cough are the prominent symptoms. The x-ray picture is that of a triangular shadow arising from the upper superior mediastinum. Primary bronchogenic carcinomas producing either lobar or lobular atelectasis of the upper lobe of the lung account for two of the main types of shadows seen on the x-ray film. A peripheral bronchogenic carcinoma arising near the mediastinum and not causing atelectasis produces an irregular paramediastinal shadow. Any of the mediastinal tumors that have been discussed may account for the fourth main type of superior sulcus tumor. Bronchoscopy rarely aids in making a positive diagnosis of tumors in this region. After a "test dose" of x-ray therapy, surgical exploration is indicated. With the exception of the benign mediastinal tumors in this location, the results of surgery have been discouraging, as in most instances the tumors are inoperable when diagnosed.

Primary tumors of the thoracic cage are characterized by pain and often the presence of a palpable mass. The pain may be in the arm, chest or abdomen. Benign tumors of the bony cage, the chondromas and osteomas, are potentially malignant and should be removed as soon as diagnosed. They present circumscribed shadows on the ribs or cartilage without evidence of bony destruction. The malignant group (osteosarcoma and the like) usually show evidence of bony destruction if extracapsular extension has occurred. Early in their course they may have been benign and at that time were operable. The results of roentgen therapy and radical surgery have been most disappointing in cases of malignant tumor of the bony cage. Therefore, as soon as a benign chest wall tumor is diagnosed it should be removed surgically, provided no valid contraindication exists.

CONCLUSIONS

1. The presence of an intrathoracic neoplasm can be usually detected by x-ray examination and bronchoscopy, the bronchoscopy taking up where the x-rays leave off. (When an intrathoracic tumor is suspected, the examination is flagrantly incomplete without the use of these diagnostic procedures.)
2. All persistent or enlarging, solitary chest wall, mediastinal or pulmonary roentgen shadows should be suspected of being neoplastic until proved otherwise.
3. All patients with the symptoms of persistent bronchial irritation or obstruction should early have the benefit of bronchoscopy. A negative bronchoscopic examination does not exclude its presence in an upper lobe or in the other lobes beyond where it can be visualized through the bronchoscope.
4. The vast majority of benign intrathoracic tumors are liable to malignant change.
5. Practically all enlarging centrally placed intrathoracic neoplasms, unless they are removed, cause death from pressure if they are benign, or from extension if they are malignant.
6. With the exception of the lymphoblastoma group, roentgen therapy is palliative and not curative. Often such therapy is needlessly prolonged until a once operable case becomes inoperable.
7. At some time during their growth most intrathoracic tumors can be removed.
8. The operative mortality is surprisingly low and is being steadily reduced as experience and improvement in surgical technic increases.
9. If the diagnosis of an intrathoracic neoplasm has been made by x-ray examination or bronchoscopy, and lymphosarcoma and metastases are ruled out, surgical exploration is at once indicated. Only a bona fide contraindication, such as cardiac decompensation, and not the apparent good general health of the patient or the reluctance of the doctor to take the responsibility, should prevent operation.

427 South Arden Boulevard.

ABSTRACT OF DISCUSSION

DR. ROY W. SCOTT, Cleveland: Lobectomy and pneumonectomy, impressive accomplishments of thoracic surgery in the past few years, have doubtless prolonged the lives of patients with lung cancer, but in interpreting results we can speak only of survival periods and not cures. Although the primary growth and local metastasis may be removed, we have no assurance that the patient is cured, since at any time up to several years bone or other metastasis may occur just as in patients with cancer elsewhere. Squamous cell cancers of the lung rarely metastasize widely and therefore offer the best prognosis from operative removal.

CAPTAIN LYMAN A. BREWER III, M. C., A. U. S.: The chairman's remarks are true that the cures in pulmonary cancer have been few as compared to the reported deaths. The reasons are (1) failure of early diagnosis and (2) lack of appreciation that early radical surgery is curative. This is an era when tumors are treated by surgery and x-rays. With the exception of intrathoracic lymphosarcoma, roentgen therapy has been singularly ineffectual. Most benign chest tumors are potentially malignant and often cause death from pressure on mediastinal structures. Therefore, until the future brings a simpler method, we must recognize that radical surgery offers the only chance of permanent cure for intrathoracic tumors

ANEURYSM OF THE RENAL ARTERY

REPORT OF A CASE

OSWALD S. LOWSLEY, M.D.
AND
EDWARD M. CANNON, M.D.
NEW YORK

Aneurysm of the renal artery is a rare clinical and pathologic entity. Medical literature contains reports of only 74 cases. The first account of a case of "renal" aneurysm was published by Dr. Daniel Nebel [1] in 1719. For two and a quarter centuries this well known case of Nebel's has been incorrectly translated and misquoted. The patient was not a physician and did not have a renal aneurysm but suffered from an aortic aneurysm. Many of the earlier papers reveal incomplete case reports and do not warrant a clinical or pathologic diagnosis of renal aneurysm. Keen [2] in 1900 and Morris,[3] also in 1900, were the first to write more extensively on the subject. Summarizing articles were published by Vogeler [4] in 1922, Conroy [5] in 1923 and Gérard [6] in 1930. Mathé [7] in 1932 wrote an excellent review of the subject and tabulated 55 cases from the literature.

It is our purpose to bring the literature up to date, report our own case (diagnosed preoperatively) and briefly review the subject. The accompanying table contains a summary of 20 cases reported in the literature since Mathé's exhaustive review; these, with the 1 presented here, bring the total number of cases to date to 75.

REPORT OF CASE

A. R., a white woman aged 47, first seen in the outpatient department (urology) of the New York Hospital on Sept. 20, 1941, complained of pain in the right flank and discomfort in the right upper quadrant. She stated that her kidney trouble had begun six years before, at which time she had "pus in the urine" and chills and fever. The pyuria and other symptoms subsided in a few weeks and she had no further trouble until July 1941, when she had dull pain in both flanks accompanied by chills and fever. The persistent gnawing pain in the right flank continued until the time of admission.

Physical examination revealed no abdominal masses. Slight tenderness was elicited in the right costovertebral angle and flank. The blood pressure was 116 systolic and 72 diastolic.

Cystoscopy and retrograde pyelography were done in the clinic. The flat plate showed both renal shadows to be normal in size, shape and position. Lying medially and outside of the right kidney was a ringlike shadow with a denser periphery and rarefaction of the center (fig. 1). The pyelogram revealed no abnormalities of the kidney proper. The area of increased density, which measured 1.5 cm. in diameter, was seen to be above the right ureteropelvic junction (fig. 2). A diagnosis of calcified aneurysm of the right renal artery was made by Dr. William E. Forsythe Jr.

The seriousness of a renal aneurysm was explained to the patient, and on October 14 she was admitted to the department of urology, James Buchanan Brady Foundation, of the New York Hospital for further study and subsequent operation.

Excretory urograms, made on the second hospital day, revealed a normally functioning upper urinary tract. The previously noted ring shaped shadow remained in the hilar region of the right kidney.

On October 20 (the sixth hospital day), under spinal anesthesia, the right kidney and renal pedicle were exposed by the usual lumbar approach. Examination and palpation of the renal pedicle disclosed a faintly pulsating, small swelling in the region of the hilus of the kidney. The lesion being definitely an aneurysm, nephrectomy was performed (fig. 3).

The patient had an uneventful recovery and was discharged on the fifteenth postoperative day. Since the nephrectomy she has been entirely relieved of the preoperative dull flank pain.

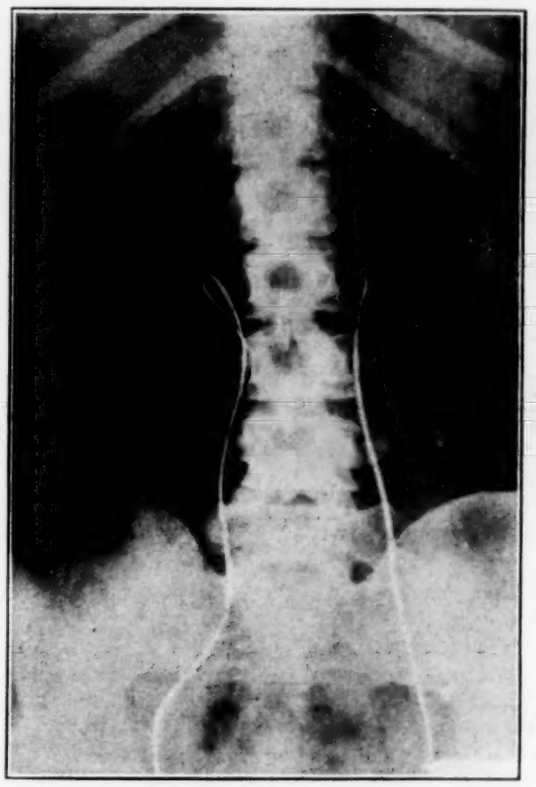

Fig. 1.—In this flat plate, medial to the right kidney shadow is a wreathlike area of increased density disrupted in one portion. This represents an aneurysm of the renal artery.

Pathologic examination of the removed kidney by one of us (E. M. C.) showed the following:

Gross: On the posterior aspect, at the bifurcation of the renal artery, was a small saccular aneurysm (fig. 4). The aneurysmal sac was yellow-red, fairly smooth in contour and firm and measured 1.4 by 1.1 by 0.9 cm. Bisection of the sac showed the aneurysmal opening to be 0.4 cm. in diameter. The orifice of the aneurysm was located on the posterior wall at the point at which the artery leaves the bifurcation to proceed to the upper pole. The wall of the sac contained calcific atheromatous plaques. A longitudinal section of the kidney showed a normal renal configuration. A few discrete, pale areas were observed in the cortex. The medullary pyramids were grossly normal in appearance, and there was no flattening of the apexes. The major calices and the pelvis were not dilated. The mucosa was smooth, and there was no evidence of tumor, ulceration or calculus.

Microscopic: Microscopic examination of the wall of the aneurysm revealed hyalinized collagenous tissue. Deposits of amorphous calcium salts were noted throughout the wall. Weigert stain showed absence of elastic tissue (fig. 5).

The pathologic diagnosis was true aneurysm of the right renal artery.

From the Department of Urology (James Buchanan Brady Foundation) of the New York Hospital.

Owing to lack of space this article has been abbreviated for publication in THE JOURNAL. The complete article appears in the authors' reprints.

Read before the Section on Urology at the Ninety-Third Annual Session of the American Medical Association, Atlantic City, N. J., June 11, 1942.

1. Nebel, Daniel: Academiae Caesareae Leopoldino Naturae Curiosorum Ephemerides, Centuria IX et X, Observations, **59:** 142, 1719.
2. Keen, W. W.: Nephrectomy for a Large Aneurysm of the Right Renal Artery, with a Résumé of the Twelve Formerly Reported Cases of Renal Aneurysm, Philadelphia, M. J. **5:** 1038, 1900.
3. Morris, H.: Aneurysm of the Renal Artery, Lancet **2:** 1002 (Oct. 6) 1900.
4. Vogeler, K.: Das Nierenaneurysma, Deutsche Ztschr. f. Chir. **176:** 297 (Dec.) 1922.
5. Conroy, M. J.: Aneurysm of Renal Artery, Ann. Surg. **78:** 628 (Nov.) 1923.
6. Gérard, M.: Contusions rénales et leurs suites éloignées, Assoc. Franç. d'urol. **30:** 172, 1930.
7. Mathé, C. P.: Aneurysm of the Renal Artery, J. Urol. **27:** 607 (June) 1932

Summary of Twenty Cases of Aneurysm of

Year	Author	Sex	Age, Years	Classification and Location	History	Symptoms	Physical Findings
1932	Mathé [7]	♂	47	True aneurysm, superior main branch of left renal artery	In 1925 fell in bathtub, striking left lumbar region; immediately passed red blood in urine; repeated attacks of left renal colic	Severe attack of left renal colic	Tenderness on deep palpation in upper left quadrant and left costovertebral angle
1934	Brinkman: J. Iowa M. Soc. **24**: 54, 1934	♀	27	.....	Sudden stablike pain in upper quadrant	Vomiting; pain in left upper quadrant; subsequent collapse; six days after discharge following exploratory operation pain recurred; occasional red blood cell in urine	Evidence of free fluid in peritoneal cavity; moderate rigidity in left renal region and left upper quadrant; urine normal
1935	Wesson and Fulmer [12]	♂	78	True aneurysm, left renal artery	Prostatectomy 2 months before for carcinoma; generalized arteriosclerosis; no trauma	Sepsis, weakness, pain in sacrum; frequency, nocturia	Cystoscopy: purulent urine from both kidneys
1936	Loughnane: Brit. J. Urol. **8**: 146, 1936	♂	55	Aneurysm, left renal artery and abdominal aorta	Colicky pains in left loin for 2 years; syphilis; malaria	Pains in left flank; frequency, nocturia	Soft mass in epigastrium; hard, pulsating mass in left loin
1937	Fircks: Zentralbl. f. Chir. **64**: 1765, 1937	♀	40	True aneurysm at bifurcation of left renal artery	Pulmonary tuberculosis (cured); no trauma	Asthenia, anemia, hematuria, symptoms of thyroid intoxication	Cachectic, hypertension—systolic 200; myoma of uterus; no other abnormal findings
1937	Kapel: Chirurg. **9**: 854, 1937	♀	57	Calcified true aneurysm, branch of left renal artery	Left abdominal distress and left renal colic	Pain in left hypochondrium and flank	Negative
1937	McKay [18]	♀	54	True aneurysm, left renal artery	Run over by a wagon; intermittent pain and discomfort in left kidney region; Wassermann negative	Pain in left side, hematuria	Pain, tenderness, spasticity on pressure over left kidney; cystoscopy: bloody reflux from left ureter; no excretion of indigocarmine from left kidney
1938	Ostling [14]	♀	24	Ruptured aneurysm, branch left renal artery	Pregnant	Sudden pain in left abdomen, vomiting, symptoms of shock and collapse	Fundus of uterus 3 fingers below xiphoid; palpable swelling in left flank
1938	Kastner: Ztschr. f. Urol. **32**: 442, 1938	♀	80	Intrarenal aneurysm, right	Episode of hematuria 6 months previous; no trauma	Suprapubic distress; severe hemorrhage from bladder	Hard, movable tumor in right lower quadrant and flank; cystoscopy: bleeding from right ureteral orifice
1938	Smith and Walkling: Bull. Ayer Clin. Lab., Pennsylvania Hosp. **3**: 203, 1938	♀	55	True aneurysm, superior polar accessory renal artery	Cholecystectomy 1931; low back pain; right upper quadrant pain	Pain in right upper quadrant	Acute tenderness in right flank and moderate tenderness in right upper quadrant
1938	Solis-Cohen and Steinbach: Radiology **31**: 173, 1938	♀	56	True aneurysm, inferior branch right renal artery	Progressive weakness; weight loss; wore support for ptosed right kidney; no trauma, pain or hematuria	Nocturia, weakness	Ptosed right kidney, with expansible mass the size of a lemon near the lower pole, transmitting a definite bruit and thrill
1939	McClelland: Tr. Am. A. Genito-Urin. Surgeons **32**: 169, 1939	♂	61	True aneurysm, intracapsular branch right renal artery	No trauma	Hematuria, 1 day only	Murmur heard in upper left abdomen; immediately under costal margin a systolic bruit with radiation to back
1939	Onell and Valencia [15]	♀	40	Ruptured true aneurysm, left renal artery	Suspicion of congenital syphilis; repeated pregnancies; glomerular nephritis; 5 months pregnant; no trauma	Lumbar pain; sudden loss of consciousness; signs of internal hemorrhage	One hour after onset, large hard mass palpable in renal fossa and extending from costal arch to iliac fossa
1940	Howard, Forbes and Lipscomb: J. Urol. **44**: 808, 1940	♀	5	Multilocular true aneurysm, left renal artery	Acute hemorrhagic nephritis at 2 years; symptoms of typical Goldblatt syndrome †	Restless, headaches	.....
1941	Howard, Suby and Harberson [9]	♀	54	False aneurysm, branch of right renal artery	Pulmonary tuberculosis; heavy feeling in right abdomen; nocturia; no trauma or renal tumor	Nervous and weak; nausea and vomiting; severe "pain in bowels"; shock	Large mass palpable in right upper quadrant extending an inch below umbilicus and to midline; later to left abdomen and down to pelvis
1941	Howard, Suby and Harberson [9]	♀	25	True aneurysm, right renal artery	Bilateral salpingo-oophorectomy and appendectomy ¶	Persistent severe tenderness in right lower abdomen	Tenderness in right lower abdomen; urine normal
	Harberson [9]			True calcified aneurysm, branch of left renal artery	Two year history of difficulty in voiding, frequency, nocturia 4-5 ×	Inability to void	Tender palpable mass in suprapubic region; prostate hard and enlarged 2 ×; blood pressure 160/100
1941	Smith [20]	♂	41	Aneurysm, right renal artery	In 1916 wounded in right loin by shrapnel; since then had aching pain in right loin	Acute discomfort in right loin; hematuria	Slight tenderness of costovertebral angle; bruit and pulsation over right loin; cystoscopic blood from right ureteral orifice
1942	Child (to be reported)	♀	33	True aneurysm, main branch right renal artery	Nine year history of intermittent pain in right upper quadrant	Pain in right upper quadrant 3 days	Blood pressure 160/100; ill defined tender mass (5 by 5 cm.) in right upper quadrant
1942	Lowsley and Cannon	♀	47	True aneurysm, right renal artery	Intermittent pain in right flank; chills and fever; pyuria 6 years	Persistent gnawing pain in right flank, slight frequency and nocturia 2 months	Slight tenderness in right costovertebral angle and flank; urine: 25 white blood cells, 2 plus clumping; culture Escherichia coli (bladder)

Additional information in footnote on page 1140.

the Renal Artery Reported from 1932 to 1942

Roentgen Findings	Diagnosis (Preoperative)	Treatment	Result	Pathologic Condition
Enlarged, irregular, left kidney; 7 calculi in upper pole; ring-shaped shadow, with a less opaque center, outside the pelvis in the parenchyma near the hilus, encroaching on the infundibulum of a dilated upper primary calix	Renal calculi; calcified renal cyst	Nephrectomy.....	Cured.....	Dilated upper calix with narrow infundibulum containing 7 hard calculi; aneurysm, superior branch of left renal artery; sac 15 mm. in diameter; calcification of aneurysmal wall; atheromatous changes in renal artery
None	Renal aneurysm	Exploratory operation; bloody fluid in peritoneal cavity; concluded hemorrhage from retroperitoneal source; nephrectomy	Cured.....	Kidney buried in huge clot
Flat plate: shadow 1.5 cm. in diameter with a dense periphery and a clearer center medial to catheter and over left 12th rib; pyelogram: shadow to medial side of left kidney at level of superior calices	Renal aneurysm	Supportive.....	Death; posteystoscopic anuria	Renal artery soft except for 1 cm. dilatation
Considerable displacement of left kidney and ureter	Undetermined; aneurysm of renal artery suspected	Laparotomy revealing both renal and abdominal aneurysm	Death in 2 months	No autopsy
Pyelogram (1932): left renal tumor; in 1936 check-up revealed tumor to have enlarged	Renal tumor	Nephrectomy.....	Improved; blood pressure fell to 130	Hypernephroma of left kidney; true aneurysm, left renal artery at bifurcation; complete lining of intima
Circular shadow within upper kidney pole, just inside renal pelvis	Calcified tuberculous focus	Nephrectomy.....	Cured.....	Nut size calcified aneurysm
Flat plate: ringlike shadow, dense periphery and central rarefaction; right pyelogram: extrarenal shadow	Undetermined	On delivering left kidney into wound, hemorrhage due to rupture of aneurysm occurred; hemorrhage controlled; nephrectomy	Death 4 days postoperatively from pneumonia and myocardial failure	Saccular aneurysm 15 by 12 mm. just proximal to bifurcation of left renal artery; wide separation of inner and outer wall, evidently a dissecting aneurysm involving sac
None	No diagnosis	Supportive.....	Death a few hours after onset	Large, left retroperitoneal hematoma *
Catheter deviated toward midline; low kidney, right; no visualization of pelvis and calices	No diagnosis	Nephrectomy.....	Cured.....	Old intrarenal aneurysm with perforation into renal pelvis; aneurysm size of small apple; wall impregnated with calcification; arteriosclerosis of vessels
Ring calculus posterior and outside right kidney	Calculus in cystic duct	Nephrectomy.....	Cured of flank pain	Saccular aneurysm 0.7 mm. in diameter, of accessory vessel; thickening of intima with calcific deposits
Extrarenal dilated pelvis, upper calix dilated; entire midsection of kidney distorted by large cystlike area with thin partly calcified wall	Aneurysm, renal artery	Nephrectomy.....	Cured.....	Large saccular aneurysm, inferior branch of renal artery, 7 cm. in diameter; wall thin and partially calcified
Circle of calcification size of 10 cent piece over right kidney and last rib; ring of calcification separate from calices but in kidney substance	.....	Nephrectomy.....	Cured.....	1 by 5 cm. cyst in upper pole; beneath capsule at lower pole a fluctuant area of blood; two large dilated vessels with thickening of walls within pelvis †
None	No diagnosis	Pulsating mass in renal fossa hemorrhaged at operation	Death 6 hours postoperative	Hazelnut-sized aneurysm of left renal artery; right kidney atrophied; microscopically left kidney showed nephrotic stage of chronic glomerular nephritis
Pyelograms negative	.....	Craniotomy; small area of necrosis in right frontal lobe; right sympathectomy §	Cured; blood pressure 5 months postoperative 125/90	Thin sacculated multilocular aneurysm of left renal artery; microscopically: chronic glomular nephritis
Large tumor in mass in right kidney area with calcification in capsule	Calcification of solitary cyst	Emergency nephrectomy; renal fascia opened with hemorrhage	Death day of operation	Aneurysmal sac adjacent to kidney measuring 25 by 9.5 cm., covered with capsule of kidney; calcification of wall
Pyelogram: slight angulation of right ureteropelvic junction	Interabdominal lesion	Laparotomy revealed a round soft collapsible pulsating mass #	Cured.....	Thimble shaped pink-gray-yellow aneurysmal sac; true aneurysm and atherosclerosis of right renal artery
No roentgen findings.....	Acute urinary retention; carcinoma of prostate; pyelonephritis; hypertension; cardiac decompensation	Supportive.....	Death.....	Carcinoma of prostate with local extension; pyelonephritis; contraction and calcification of right kidney; diverticulum of bladder; hemorrhagic cystitis; calcified aneurysm, 1 cm., of a branch of left renal artery
Loss of definition; pelvis distorted and irregular	Aneurysm of renal artery	Nephrectomy, clamp left on pedicle for 3 days	Cured.....	Aneurysm of right renal artery
Lateral and below right transverse process of first lumbar vertebra a ringlike shadow with increased peripheral density; pyelograms: normal; gallbladder series: negative	Chronic cholecystitis and cholelithiasis with hydrops	Exploratory laparotomy for a probable chronic cholecystitis; discovered a calcified pulsating small renal aneurysm; subsequent nephrectomy	Cured.....	True aneurysm (1 cm. in diameter) located at bifurcation of right renal artery; section through aneurysmal wall revealed hyalinized fibrous tissue; no elastic tissue remained; heavy deposits of lime salts
Plain x-ray: lying medially and outside right kidney, a ringlike shadow with a denser periphery disrupted in one portion and rarefaction in the center; pyelogram: increased density seen to be above the ureteropelvic junction	Aneurysm of the right renal artery	Nephrectomy.....	Cured.....	True aneurysm 1.4 by 1.1 by 0.9 cm., on posterior aspect, at the bifurcation of the right renal artery; wall of sac contained calcific atheromatous plaques; microscopic examination of the wall of the aneurysm revealed hyalinized collagenous tissue; deposits of amorphous calcium salts; absence of elastic tissue

ETIOLOGY

Most writers on aneurysm of the renal artery state that, statistically, trauma—either to the loin, back or upper part of the abdomen—is the most important causative factor. In the last century, the introduction of the germ theory, and increased knowledge of the diseases of the arterial wall itself and of congenital defects of the arteries, have produced new concepts of the etiology of aneurysms. It is doubtful whether trauma per se causes aneurysm. However, trauma may be the impetus for an aneurysmal dilatation in a renal artery which is already friable or otherwise weakened by congenital defect, infection or other disease. Gérard stated that 28 per cent of the cases reviewed by him were late sequelae of trauma to the kidney area. According to Mathé, 50 per cent of the 55 cases collected by him

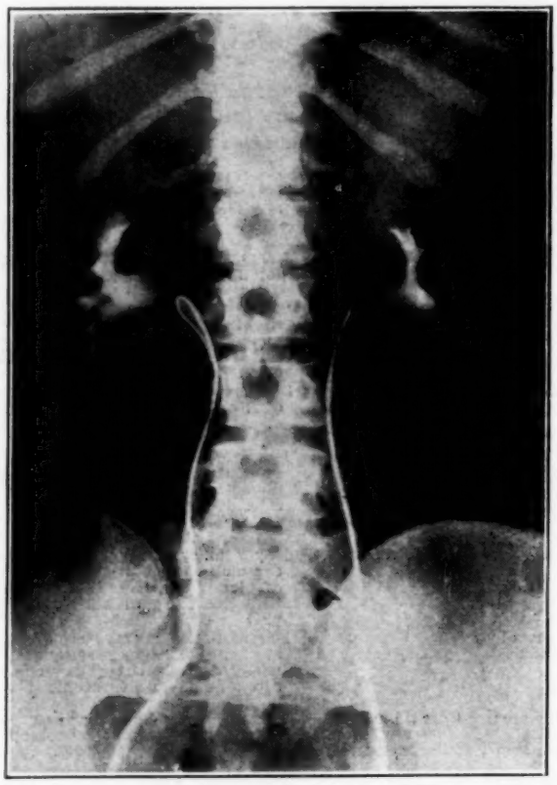

Fig. 2.—Pyeloureterogram showing, above the right ureteropelvic junction, a wreathlike shadow with a denser periphery and rarefaction of the center. The shadow is characteristic of a renal aneurysm.

presented a history of trauma. Bringing the literature up to date reduces this incidence to 33 per cent.

Intracranial saccular aneurysms occurring in the angles formed by bifurcation or branching arteries have been variously termed "congenital," "developmental," "bifurcation" and "berry" aneurysms. The exhaustive studies of Richardson and Hyland [8] have shown that "berry" and basal cerebral aneurysms are congenital and are caused by defects in elastic tissue and local defects of the media of the cerebral arteries at the apexes of the angles formed by arterial branching bifurcation. Undoubtedly, arterial wall defects occur at the bifurcation of the renal artery and play an important part in the production of renal aneurysms.

It is well known that arteriosclerosis and syphilis are important factors in the formation of aneurysms. However, these diseases have played a relatively minor role in aneurysm of the renal artery, only 4 patients in the reported series having had syphilis and 12 arteriosclerosis. Periarteritis nodosa, although occasionally generalized, displays a particular affinity for the renal artery, and a small number of cases have shown this pathologic entity at autopsy.

INCIDENCE

Judging from the number of reported cases, aneurysm of the renal artery is very rare. It might be questioned whether this rarity is actual or due to failure to recognize the lesion because of the obscurity or complete lack of signs and symptoms, were it not that autopsy records bear witness to the infrequency of its occurrence. Howard, Suby and Harberson [9] found only 10 renal aneurysms in a series of 69,819 autopsies.

Age apparently has little bearing on the incidence of this lesion. The youngest patient was 9 months and the oldest 82 years. Although 32 patients were in the fifth and sixth decades of life, it is difficult to prove that renal aneurysm of spontaneous origin is more likely to develop in this age group, since it may exist for years without producing symptoms.

Of the 72 patients whose sex was stated, 40 were males and 32 females.

PATHOLOGY

Two fundamental factors underlie the development of an aneurysm: (1) the vascular wall is weakened by congenital defect, disease or trauma, and (2) the pathogenesis is directly related to intrinsic and extrinsic vascular pressure.

Renal aneurysms are classified as "true" and "false." A true aneurysm is any pathologic localized dilatation of the artery that retains one or more of the coats of the arterial wall. Wesson [10] states that the term "false aneurysm" is a misleading one and that the diagnosis should be "traumatic spontaneous rupture of the renal artery with anatomic control of hemorrhage."

A true aneurysm is the result of a congenital defect, a vascular disease, a degenerative process or inflammatory changes of the arterial coats. Its sac is a saccular or fusiform dilatation of the wall itself. True aneurysms are usually small, ranging from the size of a pea to that of an orange. They often show calcareous deposits which are opaque to the roentgen ray. In the arteriosclerotic type of aneurysm, the beginning lesion is a subintimal plaque which progresses to implicate the vascular wall. A true arteriosclerotic aneurysm seldom perforates but, owing to its long existence and weakening of the sac, it may rupture spontaneously or perforate, from insignificant trauma, to form a false aneurysm. So long as a true saccular aneurysm remains unruptured it is not likely to produce any distinct pathologic changes. Pressure and occlusion of the aneurysm may cause thrombi and infarcts of the renal parenchyma. If the aneurysm is condensed within the capsule, it may cause some pressure necrosis.

Footnotes to table on pages 1138 and 1139:

* A branch of left renal artery dilated into a plum sized cavity bound by a partly torn connective tissue wall; sac contained an old blood clot; calcification and infection of exterior wall.

† No direct communication between pelvis and blood vessels; microscopic section showed vessels to be arteries.

‡ Hypertension 158/90-190/140; cerebral lesion and left sided paresis.

§ Decapsulation of right kidney; left sympathectomy; no drop in blood pressure; exploration revealed aneurysm of right pedicle; left nephrectomy.

¶ Laparotomy for intestinal obstruction and Meckel's diverticulum obliterated; laparotomy for lysis of adhesions; Wassermann reaction negative.

Σ This measured 1 by 1.5 cm. and consisted of right renal artery; right nephrectomy.

8. Richardson, J. C., and Hyland, H. H.: Intracranial Aneurysms, Medicine **20**: 1-83 (Feb.) 1941.

9. Howard, H. H.; Suby, H. I., and Harberson, J.: Aneurysm of the Renal Artery, J. Urol. **45**: 41 (Jan.) 1941.

10. Wesson, M. B., in discussion on papers by Howard, Suby and Harberson and by C. A. W. Uhle: J. Urol. **45**: 65 (Jan.) 1941.

False aneurysms of the renal artery are usually larger than true aneurysms. The smallest one in the published cases measured 10 by 15 cm., and Morris reported a false aneurysm which filled one half of the patient's abdomen. The wall of a false aneurysm is composed of condensed fibrous tissue developed around the extravasated and coagulated laminated blood. To this mass the surrounding structures become more or less firmly matted.

Whether a false aneurysm is formed as the result of trauma or disease, indirectly by the rupture of a saccular aneurysm or directly by the rupture of the artery, the resultant extrinsic pressure changes, displacement of organs and renal damage are the same. A false aneurysm may rupture into the peritoneal cavity, causing extensive hemorrhage. It may extend into the retroperitoneal space, rupture and form a large hematoma. Death by exsanguination may result if a false aneurysm ruptures into the renal pelvis. Blood may distend the pelvis and calices and produce complete absorption of the renal parenchyma. Partial or complete atrophy of the kidney may result from extravasated blood within the capsule. The hematoma may be entirely outside the renal capsule, and the kidney—if any of it remains—will be spread out in the wall of the sac. Blood may course along the vessels and thus gain entrance into the capsule of the kidney and then rupture into the calices.

SIGNS AND SYMPTOMS

True aneurysms present no definite syndrome of symptoms. The most constant complaint is pain referred to the upper part of the abdomen or to the lumbar region. Hematuria and the presence of a mass are infrequently observed in this type of aneurysm.

The cardinal signs and symptoms of a false aneurysm or of a ruptured aneurysm are pain, tumefaction and hematuria. Tumor masses that are progressing in size and aneurysms that have perforated give rise to pain. With slowly growing aneurysmal sacs, the pain appears only when the sac has reached a considerable size. Pain, variously described as progressive, throbbing or colicky, was present in more than 50 per cent of the reported cases.

As a true aneurysm increases in size and ruptures spontaneously or traumatically to form a false aneurysm or retroperitoneal hematoma, a tumor mass becomes palpable in the flank or upper part of the abdomen. This tumefaction may develop quickly or may be progressive over a period of months. Tumors ranging from the size of an orange to one that nearly filled the abdomen have been reported. As a rule, the mass is smooth, firm, more or less tender and fixed in position and does not move with respiration. A systolic bruit or pulsation, when present, is pathognomonic. This finding was elicited (or mentioned) in only 7 of the reported cases. The absence of a bruit or pulsation is explained by the fact that a blood clot intervenes between the inner, pulsative part of the tumor and its capsule, diminishing the impulse of the systolic waves.

Hematuria is a characteristic symptom of ruptured aneurysm when the bleeding follows trauma and precedes pain and tumefaction. It occurs when the aneurysmal sac has perforated a calix or has established a direct communication with the renal pelvis. Hematuria in cases of true aneurysm is the result of renal thrombi and subsequent infarction. The bleeding may be insignificant, but usually the hematuria is more severe than that induced by stone or neoplasm. The hemorrhage may be so extensive as to result in exsanguination, and death has occurred in 14 cases.

DIAGNOSIS

The clinical diagnosis of renal aneurysm is difficult, and in only 12 of the 75 reported cases was the condition correctly diagnosed before operation or autopsy.

Small true aneurysms rarely present symptoms and are usually discovered accidentally during investigation of the kidney, or they are found at autopsy. The usual calcific deposits in the wall of the aneurysmal sac, being opaque to roentgen rays, appear as a ringlike or wreathlike shadow on the film. This shadow is suggestive of a calcified renal aneurysm, but it must be differentiated from gallstone, renal calculus, calcified lymph gland, calcification in neoplasm, calcified cyst and calcification of autonephrectomy. Opinions differ as to the diagnostic value of this finding. Söderlund[11] and Renck[12] consider a ringlike shadow, with a dense periphery, in the region of the renal pelvis as characteristic of renal aneurysm. Wesson and Fulmer[13] state that a calcified cortex interrupted in one portion is pathognomonic. Mathé questions the value of the sign

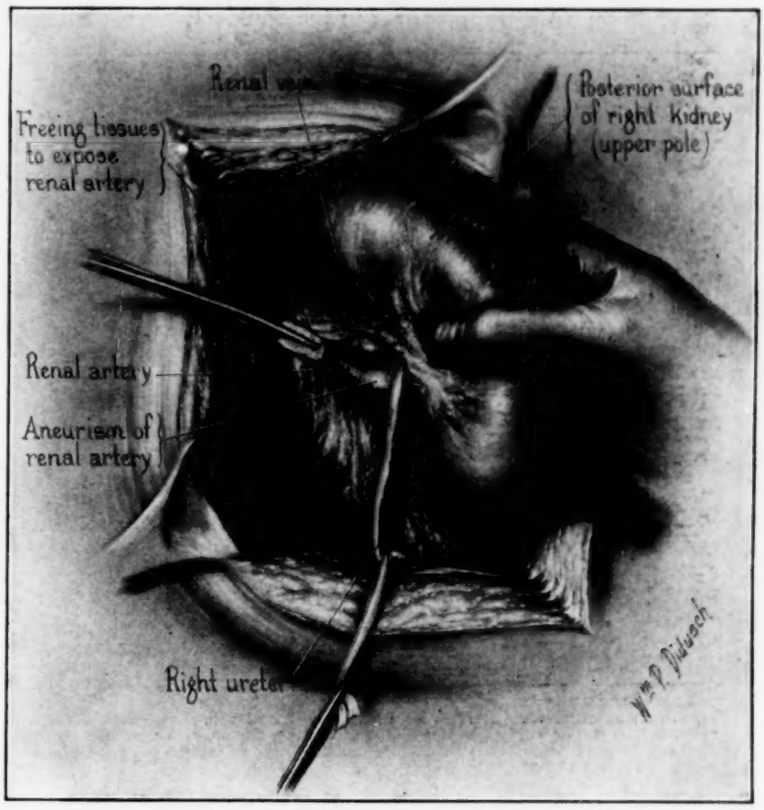
Freeing tissues to expose renal artery
Posterior surface of right kidney (upper pole)
Renal artery
Aneurism of renal artery
Right ureter

Fig. 3.—The right kidney has been exposed, showing aneurysm of the renal artery.

11. Söderlund, G.: A Case of Calcified Aneurysm of the Left Renal Artery, Nord. med. Ark. **58**: 649, 1925.
12. Renck, G.: Ueber das renalis-aneurysma, besonders vom röntgenologischen gesichtspunkt, Acta radiol. **7**: 309, 1926.
13. Wesson, M. B., and Fulmer, C. C.: Aneurysm of the Renal Artery, Am. J. Roentgenol. **33**: 176 (Feb.) 1935.

and states that the shadow cannot be differentiated from those cast by other shadow-casting lesions. A review of the literature reveals that this ringlike shadow has been reported as being present in 12 cases. In our own case, and in the cases of Söderlund and Wesson and Fulmer, the diagnosis was made on this roentgenographic finding.

The ringlike shadow cast by a renal aneurysm has been incorrectly interpreted as a calcified tuberculous focus, a neoplasm with calcification, a calcified cyst, a calcified lymph gland and a gallstone.

False aneurysms offer a particularly perplexing problem in diagnosis, for they frequently present a clinical picture similar to that of rupture of the kidney. Traumatic rupture of a false aneurysm or spontaneous perforation of a true aneurysm is to be considered in the presence of intermittent hematuria associated with excruciating pain in the loin and a rapidly or slowly enlarging immobile tender swelling in the flank. However, this syndrome may also be presented by a ruptured kidney, so that clinical differentiation is practically impossible, and only an exploratory operation can settle the question.

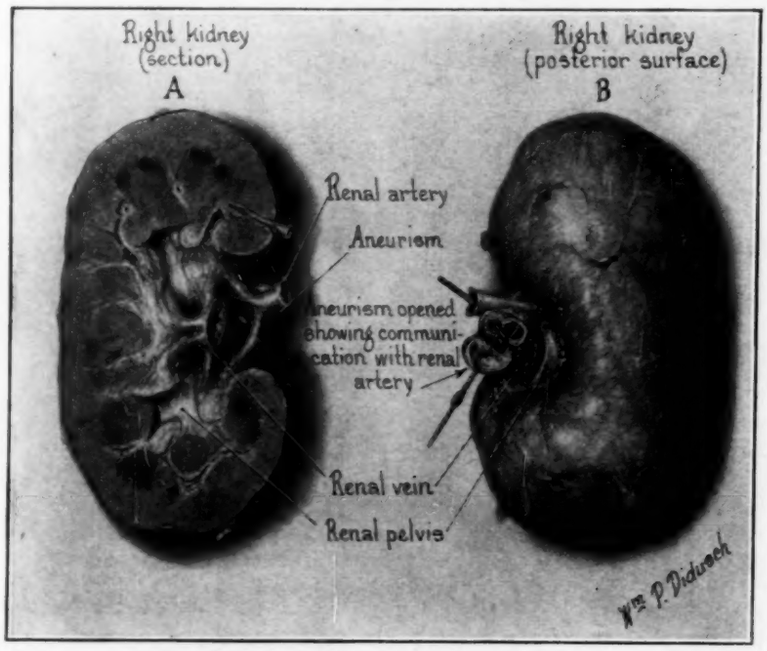

Fig. 4.—*A*, sectional view of right kidney showing renal vein and renal artery with aneurysm. *B*, posterior surface of the kidney, showing the aneurysm opened and the communication between the aneurysm and the renal artery, as indicated by the probe.

In unruptured false aneurysm, the tumor mass is the most valuable sign, with the exception of a pulsating tumor, which is pathognomonic but has been noted in only 7 cases.

PROGNOSIS

The prognosis of symptom producing aneurysms of the renal artery is grave. In the reported cases death occurred in all in which operation was not performed. The fatal outcome may be rapid, as occurred with Östling's[14] patient, who died a few hours after the onset of symptoms.

Most of the patients have died within a year of the appearance of symptoms; but some persons harboring renal aneurysms have lived for considerable periods of time before death occurred or operation was performed. Five years elapsed in Keen's and Morris's cases. The usual cause of death of patients who are not operated on is exsanguination from hemorrhage of a ruptured aneurysm into the renal pelvis, retroperitoneal tissues or peritoneal cavity. Of 37 patients who underwent operation 8 died—a mortality of 21 per cent.

TREATMENT

Procrastination in the presence of symptoms of false or ruptured aneurysm may result in the early death of the patient. Any evidence presenting itself of an enlarging perirenal hematoma, whether it is due to rupture of an aneurysmal sac, to trauma to the kidney or to any other renal pathologic condition, demands immediate surgical investigation.

The operative approach is the usual classic flank incision. If a pulsating aneurysmal sac or a perirenal hematoma is encountered, the mass should be exposed and handled very carefully, for the slightest tear in the sac may result in brisk hemorrhage. Shock and death may occur, as in the cases of Onell and Valencia.[15] As soon as the presence of an aneurysm is determined, the renal pedicle should be exposed, clamped and tied; or, if the tumor is large and hemorrhage appears inevitable, the friable pedicle should be approached transperitoneally and clamped near its branching from the aorta.

Of 37 patients operated on, 8 died. Morris's patient died after an attempt was made to extirpate the sac. Two operative deaths occurred during incision and drainage of the sac (Barnard in 1900,[16] Chisholm in 1926[17]). One postoperative death was the result of hemorrhage from the tearing of the aneurysmal sac (Onell and Valencia). McKay[18] encountered hemorrhage at operation, but the bleeding was controlled, the pedicle being clamped, cut and ligated. The patient left the operating room in good condition only to die four days later from pneumonia and myocardial failure.

Of the 29 patients treated by nephrectomy, 26 survived. Skillern[19] left pedicle clamps on because of the close relation of the aneurysm and aorta. Smith[20] encountered hemorrhage and left the pedicle clamps on for three days. Hemorrhage did not follow the removal of the clamps in either case. Orth[21] was able to evaluate the clots and successfully suture the tear in the wall of the aneurysm, and a year later he reported that the kidney was functioning satisfactorily. Callahan and Schiltz[22] extirpated a saccular aneurysm and preserved the artery.

14. Östling, K.: Ueber Aneurysmen in der Arteria renalis, lunalis und hypatica, Acta obst. et gynec. Scandinav. **18**: 444, 1938.

15. Onell, C. L., and Valencia, A. L.: Inpatient with Repeated Gravida Nephropathies and Persistent Hypertension, Rev. méd. de Chile **67**: 180, 1939.

16. Barnard H. L.: A Calcified and Cured Aneurysm of the Right Renal Artery in a Boy, Tr. Path. Soc., London **52**: 254, 1900-1901.

17. Chisholm, Alexander E.: Rupture of an Aneurysm on a Branch of the Left Renal Artery Complicating Pregnancy, Brit. M. J. **1**: 419 (March 6) 1926.

18. McKay, Robert W.: True Aneurysm of the Renal Artery, J. Urol. **37**: 783 (June) 1937.

19. Skillern, P. G., Jr.: A Case of Traumatic Aneurysm of the Right Renal Artery, with a Review of the Literature, J. A. M. A. **46**: 37 (Jan. 6) 1906.

20. Smith, Emerson: A Case of Aneurysm of the Renal Artery, Brit. J. Urol. **13**: 11 (March) 1941.

21. Orth, O.: Ein Fall von traumatischen Aneurisma der Arteria renalis sinistra, Deutsche Ztschr. f. Chir. **151**: 272 (Sept.) 1919.

22. Callahan, W. P., and Schiltz, F. H.: Aneurysm of the Renal Artery, Surg., Gynec. & Obst. **43**: 724 (Dec.) 1926.

When a unilateral true aneurysm is suspected or diagnosed roentgenographically—even though signs and symptoms are lacking—an exploratory operation should be done and, if the impression is confirmed, nephrectomy performed. Radical surgery is indicated because a small true aneurysm the wall of which is weakened and friable may rupture in the near or remote future. A calcified aneurysm may never enlarge or perforate, but nephrectomy removes the possibility.

SUMMARY AND CONCLUSIONS

1. Aneurysm of the renal artery is a rare clinical and pathologic entity. Only 75 cases have been reported to date, including a case of true aneurysm diagnosed preoperatively and presented here.

2. A congenital defect in the wall of the renal artery, particularly at its bifurcation, is a hypothetic factor in the etiology of aneurysm. It is questionable whether trauma per se produces renal aneurysm.

3. Only 12 of the 75 reported cases were suspected prior to operation or death.

4. True aneurysm is usually asymptomatic. A few patients have complained of pain in the flank. The cardinal symptoms of false aneurysm are hematuria, pain and tumefaction in the flank. The pathognomonic signs—pulsation and a systolic bruit—have been present in 7 cases. The presence in the x-ray film of a ringlike shadow, with a dense periphery disrupted in one portion and a rarefaction of the center in the kidney or hilar region, is suggestive of a renal aneurysm.

5. The treatment is surgical. In the literature, all patients presenting symptoms who were not operated on died. Of the 29 patients subjected to nephrectomy, 26 survived. Of 37 patients who underwent operation, 8 died—an operative mortality of 21 per cent.

111 East Seventy-First Street.

ABSTRACT OF DISCUSSION

DR. HERBERT H. HOWARD, Boston: There is little that I can add in the discussion of this paper. I should like to reemphasize that trauma and syphilis per se play an insignificant part in the etiology of this particular aneurysm. Arteriography by aortic injection was not mentioned by the authors in their methods of diagnosis and it seems to me that this is an important adjunct. Santos of Lisbon in 1930 was the first to publish a description of this procedure and he used a 100 per cent solution of sodium iodide. In the March 1942 issue of *Surgery, Gynecology and Obstetrics* Nelson of Seattle published an article on arteriography of abdominal organs by aortic injection using an 80 per cent solution of sodium iodide. I have used it on two occasions without any ill effects. If it is ever my good fortune to diagnose and operate in another case of true aneurysm of the renal artery I shall have as an assistant a cardiovascular surgeon to see if the aneurysm, provided it is extrarenal, cannot be operated on and the kidney saved. If one reviews the literature of true aneurysms of the renal artery, and I am speaking now of the extrarenal type, one will find the kidney to be a normal one.

DR. O. A. NELSON, Seattle: My associates and I have not encountered any aneurysm of the renal artery but we have been astounded by the large number of aneurysms, most of them found in sites that were unexpected, in our work. One of the things that was encountered frequently was blockage of one or more of the large vessels, particularly in the kidneys. I am sure that arteriography will be a procedure too that will make the diagnosis at least of aneurysm of the renal artery very easy to make. The procedure is not as hazardous as one might think.

DR. VICTOR D. LESPINASSE, Chicago: I have been looking for an aneurysm of the renal artery and never found one. I am interested in doing a reparative operation on the artery. I think that if the conditions are right it can be done. It is a feasible operation, but the condition that one must have is normal arterial wall or relatively normal arterial wall. If the wall is calcified it cannot be manipulated. One cannot sew it. It won't hold. Then one must have a method of blood control while one is making the repair. Only one clamp is needed. It isn't like an aneurysm of the femoral. But I think that point should be in anybody's mind when one operates in 1 of these cases, to try to do a reparative operation and not a destructive one. If one has that in mind I think that sooner or later somebody will be able to repair these artery aneurysms and save the kidneys.

DR. OSWALD S. LOWSLEY, New York: I am overwhelmed with joy to see our sister republics here in the audience and grouped on the table with us. I think this is very significant. I wish to commend my young associate Dr. Cannon on the splendid job that he did on this paper, which he did and I am lending my name to it. A few points I wish to emphasize. One thing in which we take a considerable amount of pride is that our resident, at that time Dr. Forsythe, made the diagnosis, and this is only one of twelve diagnoses that have been made preoperatively in the history of the world. It is rare, of course, there being only 75 cases in all the medical literature. In this particular case there was no opportunity for repair. We had it in mind at the time of operation and we hope that we shall see others and have an opportunity to repair, doing a short circuit, excising the aneurysm and leaving the artery, but in this particular case it was not possible. I came home from the meeting of the French Urological Association with enthusiasm about arteriography, and I got Dr. Henline interested. Dr. Henline operated on 16 dogs, all of which died. Now we know that a young, healthy dog will die much easier than a sick human being. If you can get by with any operation on a young, healthy dog, you can get by with that operation on a sick human being. Dos Santos told me that at that time he had done about 150 operations and only 1 patient died. This method is safe. Dr. Nelson has evidently found out how to make it safe.

Orr's Plaster Technic.—Toward the end of the war of 1914 to 1918 the American surgeon Winnett Orr made an observation which was destined to have far reaching results. Among the soldiers who were admitted to his hospital he noticed that those whose wounds had been enclosed in a plaster cast to facilitate transport to America were generally in a better condition than others who had been treated by the orthodox methods of the time. In spite of the bacterial infection present in all these cases, the granulation process was proceeding undisturbed, the patients showed no clinical sign of sepsis and the majority were doing well. This observation led him, after the war, to develop a technic of treating infections of the extremities, and in particular osteomyelitis, by the provision of drainage and complete immobilization of the limb in plaster. He also advocated this technic for infected compound fractures and later suggested that it could be applied to fractures at an early stage. His readiness to appreciate the importance of immobilization by plaster was due to his experience as a pupil of John Ridlon, who, as he writes in the preface to Orr's book Osteomyelitis and Compound Fractures (1929), for forty years had immobilized all his operative wounds of the soft tissues, as well as of bones, with plaster of paris casts and then watched the patients, not the wound.—Trueta, Josep: The Principles and Practice of War Surgery, St. Louis, C. V. Mosby Company, 1943.

DIVERTICULA OF THE COLON

PROCTOSCOPY AS AN AID IN THE DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

RAYMOND J. JACKMAN, M.D.
AND
LOUIS A. BUIE, M.D.
ROCHESTER, MINN.

Diverticula of the colon are pouchlike protrusions from the wall of the bowel which are classified as congenital and acquired. Congenital or true diverticula, of which Meckel's diverticulum is an example, are rare. Their distinguishing characteristic is that the wall of the sac contains all the normal coats of the bowel, from which the diverticulum originates. False or acquired diverticula, with which this paper is concerned, are of much more common occurrence, and their distinguishing characteristic is that the pouch is made up of mucosa and serosa; the muscular layers are absent.

These outpouchings of the colon have been a subject of discussion for a century and a half. The condition was formerly looked on as of rare occurrence, but now it is commonly encountered. Very little has been added to Cruveilhier's[1] account, which was published in 1849. We hope, herewith, to make a small contribution.

Fig. 1.—Diverticulum showing inspissated piece of stool in it.

SPECIAL VALUE OF PROCTOSCOPIC EXAMINATION

Although the diagnosis of diverticula of the colon is dependent primarily on roentgenologic studies, proctoscopic examination is of more value than may be thought. It may be of use, for instance, when a condition which roentgenologically appears to be carcinoma is actually diverticulitis. The roentgenologic filling defect following a barium sulfate enema in the presence of diverticulitis of the colon usually is described as relatively long. This is not always true, however, and if the filling defect is short the condition may be confused with carcinoma because the other roentgenologic findings in the presence of carcinoma are similar to those of diverticulitis, especially when the carcinoma is associated with inflammation. Proctoscopic examination may make the diagnosis possible.

Not uncommonly, moreover, differential diagnosis between a malignant condition and inflammation is difficult or impossible, even at the time that the surgeon explores the abdomen. In those cases in which colostomy has been performed, proctoscopic examination of the distal segment of bowel by way of the anus, as well as examination of both proximal and distal segments through the colonic stoma, is of inestimable value in determining the degree of the inflammatory process and the amount of obstruction in the region of inflammation. The surgeon must be informed concerning these matters before he attempts closure of the colonic stoma.

Proctoscopic Signs.—In 1939 one of us[2] reported five proctoscopic signs which may determine, or lead to the strong suspicion of, the presence of diverticulosis or diverticulitis. The signs enumerated are as follows:

1. Limited mobility of a segment of bowel which is normally freely movable. Relative immobility of a segment of bowel alone is insufficient evidence on which to base a diagnosis of diverticulitis, but when this is associated with one or more of the other irregularities mentioned immobility forms strong supportive evidence. A fixed or retroverted uterus and pelvic inflammatory disease may interfere with, or even prevent, complete proctoscopic examination. It is not difficult to distinguish this type of immobility from that which is observed in the sigmoid from which inflamed diverticula originate. In those instances in which the interference is caused by pelvic disease or a fixed, retroverted uterus, the obstruction is confined to the rectum. Usually in diverticulitis the rectum is unobstructed, and little difficulty is experienced with the examination until the sigmoidal segment is reached.

2. Angulation of the bowel. The lumen may turn sharply at the point at which it is immobilized by diverticulitis, and advancement of a proctoscope of average caliber beyond the angulation may be difficult or impossible.

3. Reduced lumen and adherent mucosal folds. The contracture of the lumen is due to impingement on the wall of the bowel and as the lining membrane is crowded together the mucosal folds become adherent. The mucosa may be edematous. Often additional information can be gained by using an instrument of smaller caliber.

4. Sigmoidal sacculation. This peculiarity is characterized by the appearance of shallow pouches which extend partially, or wholly, around the wall of the bowel. The pouches are separated by ridgelike elevations; usually they are observed in a mobile sigmoid which bears no evidence of inflammatory disease. Frequently these sacculations are found in the course of postmortem examination of elderly persons. Spriggs and Marxer,[3] after making roentgenologic studies of the colon, described a prediverticular state in which normal segmentation of the bowel is absent and is replaced by a ragged outline of little convex irregularities. It is doubtful whether the prediverticular stage of Spriggs and Marxer is identical with the sacculation seen in proctoscopic examination and so frequently observed in postmortem examination of elderly persons.

5. Seeing the diverticula (fig. 1). One or more diverticula are actually seen more frequently than is generally believed. Whenever it is possible to discover a diverticulum, however, inflammation seldom is present.

STUDY OF FOUR HUNDRED CASES

The records of 400 consecutive patients of the Mayo Clinic who were found to have diverticula of the colon were studied in order to compare the proctoscopic with the roentgenologic findings and, in this connection, to determine the value of the signs enumerated. Of these patients, 213 (53 per cent) were males and 187 (47 per cent) were females. Their average age was 56 years.

From the Section on Proctology, Mayo Clinic.
Read before the Section on Gastro-Enterology and Proctology at the Ninety-Third Annual Session of the American Medical Association, Atlantic City, N. J., June 10, 1942.

1. Cruveilhier, Jean: Traité d'anatomie pathologique générale, Paris, J. B. Baillière, 1849, vol. 1.

2. Buie, L. A.: Diverticula of the Colon, New England J. Med. **221**: 593-598 (Oct. 19) 1939.

3. Spriggs, E. I., and Marxer, O. A.: Intestinal Diverticula, Quart. J. Med. **19**: 1-34 (Oct.) 1925.

In 150 (38 per cent) of the 400 cases proctoscopic examination was not performed and the diagnosis was made from clinical and roentgenologic studies only (table 1). In 8 (2 per cent) of the 400 cases roentgenologic examination of the colon was not carried out and the diagnosis was made by clinical and proctoscopic examinations only. The diverticula were seen at proctoscopic examination in all 8 cases. It is with the remaining 242 cases (60 per cent) of the 400 cases, in which both sigmoidoscopic and roentgenologic studies of the colon were carried out, that this study is primarily concerned.

Of the 242 cases, results of sigmoidoscopic examination were negative in 82 (34 per cent) (table 2). In the remaining 160 cases (66 per cent) of 242 some evidence of the existence of diverticula was ascertained by sigmoidoscopic examination or the diverticula were seen.

In 35 (22 per cent) of the 160 cases, diverticula were observed on sigmoidoscopic examination and their presence was confirmed by roentgenologic studies of the colon (table 3). In an additional 72 (45 per cent) of the 160 cases the proctoscopist reported the presence

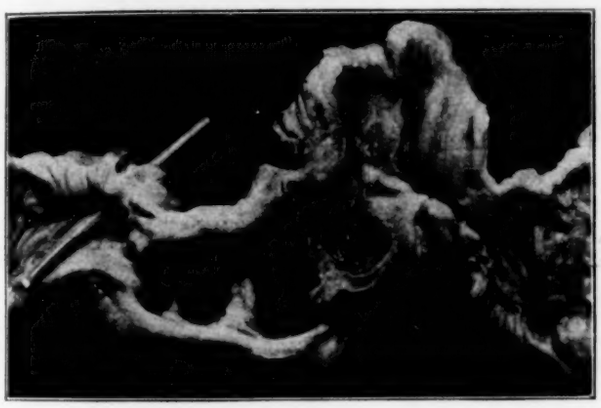

Fig. 2.—Portion of resected sigmoid showing sacculation, diverticula and strong perisigmoidal inflammatory reaction.

of sacculations of the sigmoid and the roentgenologist confirmed his suspicion as to the presence of diverticula. Parenthetically, it can be said that in 18 of the 35 cases in which diverticula were seen sacculations were seen also, making a total of 90 cases in which sacculations were observed (fig. 2). In the 53 cases (33 per cent of the 160) which remained after the 35 and 72 had been subtracted, there was other sigmoidoscopic evidence which strongly suggested the presence of diverticula of the sigmoid, and roentgenologic studies of the colon confirmed the diagnosis. These findings were immobility, sharp angulation, narrowing of the lumen, mucosal edema, extrarectal mass and inability to pass the proctoscope the average distance. Although these findings may exist singly, they usually exist in combination.

It is interesting to observe that in 3 of the cases of colonic diverticula sacculations were noticed on proctoscopic examination, but the primary roentgenographic studies failed to reveal the presence of diverticula. From one to six years later roentgenologic studies of the colon revealed the presence of diverticula. It is possible, in many of the cases in which sacculations are found on proctoscopic examination, and in which diverticula cannot be demonstrated by roentgenologic studies, that these sacculations may represent a prediverticular stage.

PROCTOSCOPY AFTER COLOSTOMY

Early in this paper we pointed out the value of proctoscopic examination following colostomy. With present day medical management the use of colostomy or other emergency operation for relieving obstruction

TABLE 1.—*Four Hundred Cases in Which Diverticula Were Found*

Method of Diagnosis	Number	Per Cent
Clinical and roentgenologic only	150	38
Clinical and proctoscopic only	8	2
Proctoscopic and roentgenologic	242	60
Total	400	100

TABLE 2.—*Two Hundred and Forty-Two Cases in Which Diverticula Were Found and Both Sigmoidoscopic and Roentgenologic Examinations Were Performed*

Result of Sigmoidoscopic Examination	Number	Per Cent
Negative	82	34
Revealed, or gave some evidence of diverticula	160	66
Total	242	100

of the lower part of the bowel has decreased considerably. There are, however, definite indications for colostomy, namely (1) acute obstruction which has failed to respond to medical management, (2) sigmoidovesical fistula and (3) extensive abscess formation. It is in these complicated conditions that preoperative diagnosis by proctoscopy is of great value.

Special Study of Fifty Cases.—We selected for special study 50 patients on whom colostomy had been performed because of an obstructing lesion in the lower part of the bowel and in relation to which a preoperative diagnosis was impossible. The nature of the obstruction was indeterminate for the following reasons: 1. The problem was of an emergency character. Many

TABLE 3.—*One Hundred and Sixty Cases in Which Positive or Suspicious Sigmoidoscopic Findings Were Confirmed Roentgenologically*

Result of Sigmoidoscopic Examination	Number	Per Cent
Diverticula seen (in 18, sacculations also seen)	35	22
Sacculations seen; diverticula suspected	72	45
Other suggestive sigmoidoscopic evidence	53	33
Total	160	100

TABLE 4.—*Fifty Cases in Which Examination Was Made After Colostomy*

Method of Diagnosis	Cases	Per Cent
Proctoscopic	37	74
Pathologic	13	26
Total	50	100

patients were too sick to permit necessary diagnostic examinations to be made. 2. The attempt to relieve obstruction by medical management failed. 3. Colostomy had been performed as an emergency elsewhere. Thirty-one of the patients had been operated on at the clinic and 19 elsewhere. In many of these cases, even though the abdomen was explored at the time of colostomy, the surgeon was unable to determine the nature of the obstruction. Proctoscopic examination

by way of the colonic stoma or anus was responsible for making a diagnosis in 37 (74 per cent) of these cases (table 4). In many cases the examination had to be repeated several times, at intervals of several days or weeks, and often it was found that a loop of bowel which was found to be inaccessible at one examination because of fixation and inflammation had become, at a subsequent examination, more mobile, thus permitting more satisfactory examination. In the remaining approximately one fourth of the cases the diagnosis was made by the pathologist after the diseased segment of bowel had been resected (fig. 3).

SUMMARY

A study of 400 cases of diverticula of the colon has been made. The diagnosis was made clinically and by roentgenologic examinations in 150 of the cases and clinically and by proctoscopic examination in 8. In the remaining 242 cases both roentgenologic studies of the colon and sigmoidoscopic examinations were performed. In 160 of these 242 cases sigmoidoscopic examination revealed or gave some evidence of the presence of diverticula. Of these 160 cases, in 35 the proctoscopist saw diverticula (sacculations also in 18 of the 35); in 72 sacculations and in 53 one or more of the following evidences: immobility, sharp angulation, narrowing of the lumen, mucosal edema, extrarectal mass or inability to pass the proctoscope the average distance.

In another group of 50 cases in which colostomy had been performed as an emergency measure because of an obstructing lesion in the lower part of the bowel, and in which the preoperative diagnosis was indeterminate, a study was made in order to learn the value of sigmoidoscopic examination performed by way of the anus or the colonic stoma. Sigmoidoscopic examination was responsible for the diagnosis in 37 of the 50 cases.

CONCLUSIONS

1. Roentgenology provides the most valuable single aid in establishing the diagnosis of diverticula of the colon.

2. The most valuable single proctoscopic finding, aside from actually seeing the diverticula, is the presence of sacculations.

3. The proctoscopic findings of immobility of the bowel, angulation, mucosal edema, narrowed lumen and extrarectal mass are of value, but it should be remembered that some of these signs are observed in other diseases of the pelvic organs.

4. Our study would indicate that proctoscopy is a valuable adjunct to clinical and roentgenologic findings in determining the nature of obstructive lesions in the lower part of the bowel.

ABSTRACT OF DISCUSSION

DR. JOHANNES PESSEL, Trenton, N. J.: At the Graduate Hospital we don't see these diverticula quite as frequently as do Drs. Jackman and Buie. We do, however, notice edema. Our experience is that edema below malignant lesions is rare, and when it occurs we suspect an inflammatory lesion. We have found a longer proctoscope helpful, that is, preoperatively. We frequently use a 14 or 16 inch proctoscope in an attempt to view this area. I should like to mention the use of some form of atropine or belladonna for a day or two previous to a second examination. This frequently will at least diminish the amount of spasm that one encounters on the first examination and one can get a better impression of the lesion.

DR. JOHN C. M. BRUST, Syracuse, N. Y.: The menace of malignancy is constantly present and must if possible be excluded. Medical students are far too often taught that diverticulitis is merely "left sided appendicitis." The frequency of bladder symptoms, rare instances of sudden profuse rectal bleeding, absence of fever and many other features combine to make diverticulitis a complex and often bizarre picture. One brief case report will illustrate many of these points: A man aged 52 had rectal pain and inability to void. The duration of illness was thirty hours. Catheterization was performed and 950 cc. of concentrated urine obtained. The prostate felt normal. There was induration and tenderness felt "through" the posterior rectal wall in the hollow of the sacrum. The abdomen was soft and the bowel history was that of prolonged constipation. The day after admission there was increasing evidence of fluctuation between the sacrum and the rectum. No intrinsic lesion was seen by sigmoidoscopy for 20 cm. This procedure was done under caudal anesthesia because of rectal pain. A stab wound was made through an operating anoscope and a hemostat passed behind the rectum through the rectal mucosa. A moderate amount of foul pus was obtained and from this retrorectal abscess cavity we obtained hundreds of tiny fecaliths about the size of grape seeds. A barium sulfate enema with a roentgenogram of the colon revealed narrowing at a point in the lower sigmoid but it did not appear malignant. No diverticula were seen. We felt that a diverticulum had perforated and an abscess had formed. The contents of the diverticulum could account for the innumerable small fecal pellets. Despite sulfanilamide therapy and general supportive and dietary measures, he continued to have retrorectal tenderness and a persistent discharge of pus. Twelve days after admission the abdomen was opened. An infected mass was found surrounding the lower sigmoid. The inflammatory reaction was pronounced. It did not feel or appear malignant. A double barreled colostomy was performed. Hot irrigations were begun. Sulfanilamide therapy was continued. We kept this man under observation and used a proctoscope at frequent intervals. We believe this was a perforation of a solitary diverticulum in the lower sigmoid. The severe reaction prevented any actual demonstration of an opening by proctoscopy but we could say with assurance that no malignancy existed. We rarely see diverticular openings if an acute inflammatory process is present. The other signs, namely sigmoidal sacculation, limited mobility, sharp angulation and reduced lumen, are of dubious value. Sigmoidoscopy properly performed is rarely productive of severe pain. One exception is acute diverticulitis.

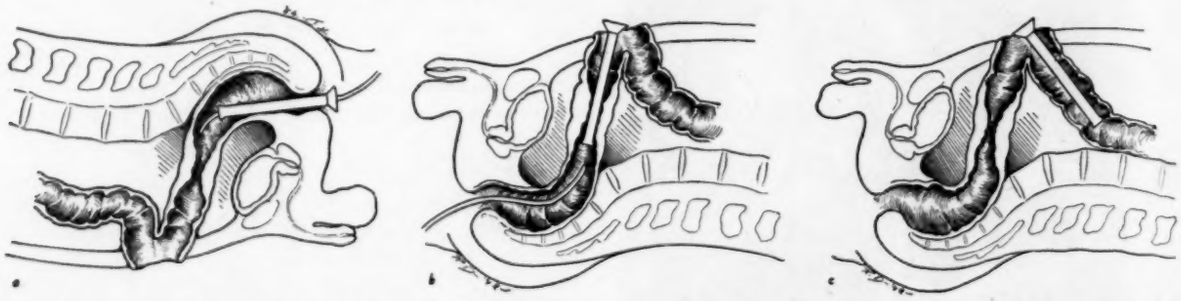

Fig. 3.—Method of examination with sigmoidoscope after colostomy: *a*, sigmoidoscope inserted by way of anus and rectum, leaving catheter in place to indicate that that much of the bowel was examined; *b*, sigmoidoscope inserted by way of stoma, catheter seen, indicating that the distal segment has been completely examined; *c*, examination of the proximal loop by way of stoma.

THE PREVENTION OF RENAL OBSTRUCTION DURING SULFADIAZINE THERAPY

CHARLES L. FOX JR., M.D.
OLE J. JENSEN JR., M.D.
NEW YORK
AND
LIEUTENANT GILBERT H. MUDGE
MEDICAL CORPS, ARMY OF THE UNITED STATES

In the recent literature there are many reports of renal obstruction during therapy with sulfapyridine, sulfathiazole and sulfadiazine. This complication is attributed to the poor solubility of these drugs and their acetyl derivatives.[1] It is important to realize that the sulfonamide compounds differ considerably in their solubility. Sulfanilamide, for example, is a relatively soluble drug, and renal complications are rare. Sulfapyridine, sulfathiazole, sulfadiazine and their acetyl forms, on the other hand, are relatively insoluble [2] and renal complications occur frequently. If the solubility of these drugs in urine could be increased, this complication might be prevented. The data presented here will show that the solubility of sulfathiazole and sulfadiazine and their acetyl forms can be increased and renal precipitation thereby prevented.

The first procedure in our studies was to determine the solubility of sulfathiazole and sulfadiazine and their acetyl derivatives in normal human urine over the p_H range 5.0 to 8.0.[3] This proved to be the key to the problem; as seen clearly in figure 1, there is a very sudden and decided increase in the solubility of these substances as the urine is made alkaline. The explanation of this phenomenon is that these drugs and their acetyl derivatives are weak acids which ionize and form soluble salts in an alkaline medium [4] (e. g. sodium sulfadiazine and sodium acetyl sulfadiazine). The question then arises How much soluble salt formation can occur in urine within the physiologic p_H range? As the p_H is raised from 5.0 to 7.0 (fig. 1) there is little salt formation and the solubility in urine is not appreciably increased; from p_H 7.0 to 8.0, however, there is extensive salt formation and the solubility of sulfathiazole and sulfadiazine, both free and acetyl, is greatly increased.[5] In the case of sulfapyridine and its acetyl form, on the other hand, extensive salt formation does not occur until p_H 9.0 and 10.0 respectively are reached —beyond the p_H range of urine; this accounts for the failure of alkali therapy to prevent renal precipitation of this drug. With sulfanilamide, salt formation does not occur until p_H 10.6 is reached; but, in contrast to the preceding drugs, it is a relatively soluble substance.

In vivo this phenomenon has also been investigated in dogs.[6] In these experiments it was found that sulfadiazine crystalluria was produced when acid urine was excreted after the administration of ammonium chloride; conversely, crystalluria was prevented by maintaining the urine alkaline by the administration of sodium bicarbonate. Furthermore, it was noted that the p_H of the urine closely regulated the concentration of sulfadiazine that was excreted in solution in the urine; i. e., low levels were obtained in acid urine and high levels in alkaline urine during constant drug dosage.

In a study of the pathogenesis of complications in the urinary tract it is important to consider the concentration at which the drug is excreted in the urine. While blood levels of about 10 mg. per hundred cubic centimeters are obtained in patients receiving 4 to 6 Gm. a day, the level that is obtained in the urine varies from 100 to 300 mg. per hundred cubic centimeters. Increasing the urinary output from 1,000 to 2,000 cc. a day might double the quantity of sulfadiazine in solution, but raising the p_H from 6.5 to 7.5 will permit more than a tenfold increase in solubility.

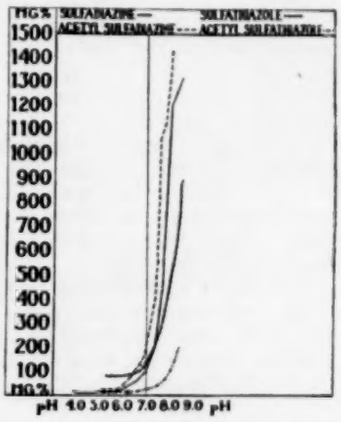

Fig. 1.—The variation in the solubility of sulfadiazine and sufathiazole and their acetyl forms in normal human urine from p_H 5.0 to 8.5. Horizontal axis: Hydrogen ion concentration (p_H) of the urine at which drug levels were determined. Vertical axis: concentration of drug in the urine (milligrams per hundred cubic centimeters) showing the great increase in the solubility of these substances in alkaline urine.

In view of the in vitro experiments indicating the greatly increased solubility of sulfathiazole, sulfadiazine and their acetyl derivatives in alkaline urine and the animal experiments substantiating this, it was decided to employ this method in the massive sulfadiazine therapy of subacute bacterial endocarditis in the hope that the renal complications with oliguria reported by Dick [7] might be prevented.

CLINICAL PROCEDURE

Two patients whose diagnosis of subacute bacterial endocarditis was established were selected for massive sulfadiazine therapy. To induce diuresis of an alkaline urine, sodium bicarbonate [8] and large amounts of fluids were given prior to the administration of sulfadiazine. The p_H of each specimen was measured as soon as voided with a Beckman p_H meter and if the p_H of the urine had dropped below 7.5 additional alkali was administered. Each specimen was centrifuged and the

Dr. Charles Roh and Miss Margaret Boyle cooperated.

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From the Department of Bacteriology, Columbia University College of Physicians and Surgeons, the Squier Urological Clinic and the Department of Medicine, Presbyterian Hospital.

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5. Because the degree of ionization is dependent on the concentration and nature of buffer present, which will vary with individual specimens, solubilities slightly different from these may be reported from other studies. Acetyl sulfadiazine is only very slightly more soluble in water than sulfadiazine in water; 15 cf. 12 mg. per hundred cubic centimeters. It is, however, a stronger acid than any of these compounds and hence becomes more soluble than any (except sulfanilamide itself) as the p_H is raised and salt formation occurs.

6. Jensen, O. J., Jr.: Factors Controlling Renal Excretion of Sulfonamides, thesis, Squier Urologic Clinic, Presbyterian Hospital, New York.

7. Dick, G. F.: Subacute Bacterial Endocarditis: Recovery Following Intravenous Sodium Sulfadiazine, J. A. M. A. **120:** 24 (Sept. 5) 1942.

8. Some potassium bicarbonate was given to prevent the accumulation of excess sodium ion and consequent edema. The potassium salt, however, produced nausea and vomiting and was discontinued. No edema or alkalosis resulted from the large amounts of sodium bicarbonate administered.

sediment examined microscopically for drug crystals. When crystals were observed a rough quantitative estimate of the degree of crystalluria was obtained by determining the concentration of sulfadiazine in the sediment and in the supernatant fluid.[9] When these differed by more than 5 per cent crystalluria was grossly visible. Renal function tests were done before and after treatment; the specimens were tested for albumin and the specific gravity was measured.

The Renal Function Before and After Massive Sulfadiazine Therapy

Case	Maximum Specific Gravity		Albumin		Casts or Blood Cells		P. S. P. Excretion in 2 Hours		Serum Urea Nitrogen Mg./100 Cc.	
	Before	After	Before	After	Before	After	Before	After	Before	After
1	1.024	1.020	0-+	0-+	0	0	65% in 255 cc.	60% in 180 cc.	17	13
2	1.020	1.024	0	0	0	0	70% in 545 cc.	80% in 390 cc.	10	12

REPORT OF CASES

CASE 1.—R. W., a white man aged 34, had fever, night sweats, malaise and weight loss of two months' duration, a history of rheumatic fever and chorea, signs of mitral stenosis and insufficiency and aortic insufficiency. Blood cultures contained a strain of Streptococcus viridans. The only signs of cardiac decompensation were a slightly enlarged liver and moderate dyspnea on exertion. There was no anemia. Before admission to the hospital he had received sulfathiazole in normal therapeutic amounts for two weeks with slight symptomatic improvement. Renal function tests were normal and are shown in the accompanying table.

Preparatory alkali therapy consisted in the oral administration of 5.4 Gm. of sodium bicarbonate daily. After five days, however, this was insufficient to make the urine persistently alkaline; therefore 12 Gm. of potassium bicarbonate was given on the day before and on the day of treatment. At the start

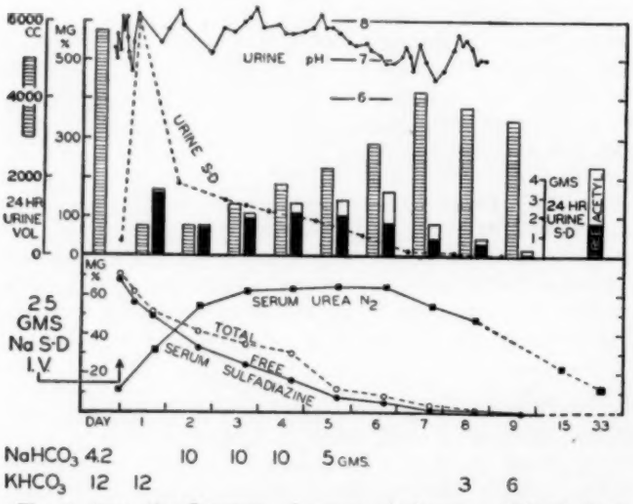

Fig. 2 (case 1).—Summary of course of therapy. Although large quantities of sodium bicarbonate were given, certain specimens of urine became acid. The minimum daily output of urine was 775 cc. The blood and urine sulfadiazine levels are shown as well as the transient rise in serum urea nitrogen. The highest sulfadiazine levels in the urine did not greatly exceed the levels found during routine therapy.

of therapy the urine p_H was 7.65. Fluids were forced and the day before treatment the patient voided 5,730 cc. Twenty-five Gm. of sodium sulfadiazine (0.454 Gm. per kilogram of body weight) was administered intravenously in 500 cc. of distilled water over a period of one hour and twenty minutes. A serum level taken one hour after the infusion had been terminated was 69.5 mg. of sulfadiazine per hundred cubic centimeters (fig. 2). For several hours thereafter the patient had frequency and burning on urination with moderately severe pain in the flank, hematuria and crystalluria. It is noteworthy that at the time these symptoms began the urine p_H had fallen, varying from 6.6 to 7.46, and that the urine sulfadiazine concentration was 639 mg. per hundred cubic centimeters, which is well above the solubility found in vitro at the p_H of the individual voiding (fig. 1). At the same time the specific gravity of the urine varied from 1.002 to 1.006. Larger doses of potassium bicarbonate were given and the urine p_H was raised, varying from 7.4 to 8.1 for the next day, with slight crystalluria persisting for that day. Sodium bicarbonate was then given intravenously on the following days. There was no oliguria, as shown by a minimum daily volume of urine of 775 cc. This is in sharp contrast to the twenty-four urine volume of 15 cc. reported by Dick.[7] For the following three days the patient had gross hematuria and 2 to 3 plus albuminuria. Microscopic hematuria and 1 to 2 plus albuminuria persisted for

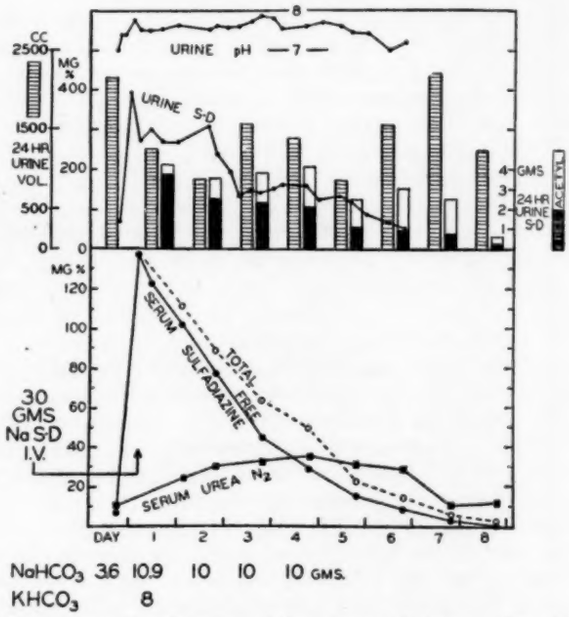

Fig. 3 (case 2).—Summary of first course of therapy. The administration of large amounts of sodium bicarbonate kept the urine alkaline. The minimum daily output of urine was 860 cc. The blood and urine sulfadiazine levels are also shown, together with the transient rise in serum urea nitrogen. The highest sulfadiazine levels in the urine did not greatly exceed those found during routine therapy.

three days more. The serum urea nitrogen rose to 64 mg. per hundred cubic centimeters on the fourth day and then gradually returned to normal. During the period of treatment the patient experienced slight nausea and vomiting, his temperature remained elevated and there were many embolic phenomena, whereas previously there had been but few. The blood cultures (with para-amino benzoic acid added to the mediums) were negative for one week and then again became positive.

CASE 2.—B. B., a white schoolgirl aged 16, had fever, malaise and an occasional sore finger tip for two months, a history of rheumatic fever, signs of mitral stenosis and insufficiency and aortic insufficiency; blood cultures yielded a strain of Streptococcus viridans. There was no evidence of cardiac decompensation. Prior to admission to the hospital she had received sulfadiazine in the usual doses for a total of two weeks, with temporary symptomatic improvement. There was no anemia and the renal function tests were normal, as shown in the table.

Preparatory alkali therapy consisted in the oral administration of 4.5 Gm. of sodium bicarbonate and 8.0 Gm. of potassium bicarbonate for two days. At the start of therapy the p_H was

9. The sulfonamide levels were determined by the method of Bratton and Marshall (A New Coupling Component for Sulfanilamide Determination, J. Biol. Chem. **128**: 537 [May] 1939) with the Klett-Summersen photoelectric colorimeter.

7.75. Fluids were forced and a diuresis of 2,150 cc. was obtained. Thirty Gm. of sodium sulfadiazine (0.52 Gm. per kilogram of body weight) was given intravenously in 600 cc. of distilled water over a period of one and one-half hours. One hour after the infusion was terminated the serum sulfadiazine level was 138 mg. per hundred cubic centimeters (fig. 3). The patient had no specific urinary symptoms but experienced slight discomfort in the left upper quadrant of the abdomen similar to that which she had noted before the administration of sulfadiazine. Nausea and vomiting appeared after the termination of the infusion and lasted one week. The daily fluid balance was maintained by the administration of parenteral fluids. There was gross hematuria and 2 to 3 plus albuminuria for three days. The p_H of the urine remained above 7.5 and there was no oliguria—the minimum daily volume of urine was 860 cc. Sodium bicarbonate (10 Gm. a day) was given intravenously for the next four days in the late evening in an attempt to counteract the usual acidity of the early morning specimens. Microscopic hematuria and 1 plus albuminuria were noted in the next three days. A rare sulfadiazine crystal was seen in only one of the urine specimens during the week following the infusion of the drug, and during this period all of the urine sulfadiazine levels fell within the in vitro solubility curve (fig. 3). The serum urea nitrogen was 36 mg. per hundred cubic centimeters on the fourth day after treatment and returned to normal on the seventh day. Renal function studies after massive sulfadiazine therapy were normal (table 1).

Following the massive intravenous dose of sulfadiazine the patient had a normal temperature and negative blood cultures for one week, but then fever reappeared and the blood cultures became positive. Although the single massive dose had not been followed by oliguria, there was definite evidence of temporary disturbance of renal function. Accordingly, smaller daily doses of the drug were given. There was no reaction to a trial dose of 1 Gm. of sulfadiazine, and, after fluids had been forced and the urine had been made alkaline, 10 Gm. of sodium sulfadiazine was given intravenously (fig. 4). A serum level of 38.3 mg. per hundred cubic centimeters was obtained, and on the following day 10 Gm. was again given intravenously, and one hour later the serum level was 54.5 mg. per hundred cubic centimeters. Transient hematuria and albuminuria followed both infusions. The serum level fell rapidly and it was therefore decided that a uniformly higher serum level could be maintained with large divided oral doses. After another infusion of 5 Gm. of the sodium salt, the patient was maintained on daily doses of from 8 to 20 Gm. of sulfadiazine for seventeen days, the average dose being 13.7 Gm. a day (0.25 Gm. per kilogram of body weight). The average serum sulfadiazine level was 25 mg. per hundred cubic centimeters and the daily urine volume varied from 1,200 to 3,300 cc. with the exception of the final day of treatment. The average daily intake of sodium bicarbonate was 12.1 Gm. There was no edema or clinical evidence of alkalosis, and the serum carbon dioxide combining power varied from 53.2 to 72.7 volumes per cent. The urine p_H was maintained above 7.5 with the exception of the first voiding each morning, which ranged from 6.4 to 7.4 (average 7.0), despite the administration of as much as 3.6 Gm. of sodium bicarbonate at 2 a. m. During this period, there was gross crystalluria on six occasions but no flank pain, dysuria or hematuria occurred. The serum urea nitrogen was not elevated, and repeated urea clearance tests were normal. On the seventeenth day of therapy crystalluria with hematuria, flank pain and dysuria developed. At this time the level of sulfadiazine in the urine was 445 mg. per hundred cubic centimeters but the p_H was only 7.0, which is not high enough to keep this concentration of sulfadiazine in solution (fig. 1). Sulfadiazine was stopped but the administration of sodium bicarbonate was continued, and the hematuria and flank pain subsided in one day. The urine volume fell to 750 cc. for one day, but there was no nitrogen retention. Following this episode an intravenous pyelogram showed normal excretion from both kidneys without filling defects. During the seventeen day period the patient was afebrile, but following cessation of the drug, fever reappeared and the blood cultures once again became positive.[10]

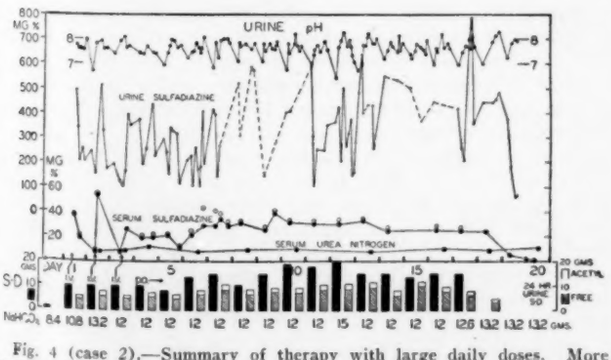

Fig. 4 (case 2).—Summary of therapy with large daily doses. More constant high serum levels of sulfadiazine resulted from divided oral dosage. Higher urinary levels (crystal free) were obtained with this form of therapy. The large daily doses of sodium bicarbonate needed to keep the urine alkaline are shown. The serum urea nitrogen did not become elevated.

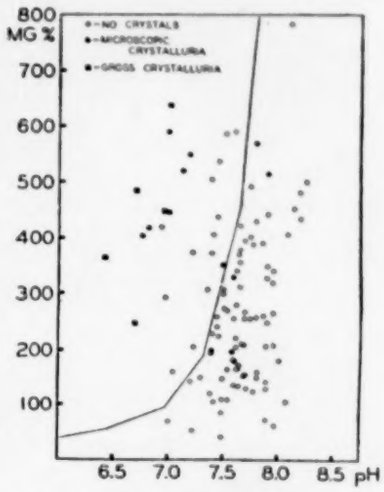

Fig. 5.—The occurrence of crystalluria in relation to the p_H and drug concentration of the voided urine. The solid curve is the in vitro solubility of sulfadiazine from figure 1. Gross crystalluria occurred when the p_H was lower than (to the left of) the in vitro solubility curve. Of the specimens to the right of this curve which contained crystals, one half were voided immediately after a specimen to the left of the curve containing gross crystals.

COMMENT

It is apparent that in these 2 cases renal obstruction during massive sulfadiazine therapy was prevented. The role of p_H in preventing crystalluria is clearly demonstrated by figure 5, which relates the p_H and drug level of each specimen to crystalluria. It has been shown that the solubility of sulfadiazine in vitro in human urine can be increased many times by increasing the p_H. Figure 5 shows that this applies also to human urine excreted during therapy. In comparing these specimens with the in vitro solubility curve, it will be seen that 48 per cent of the specimens in which the p_H was lower than (to the left of) the solubility curve contained gross or microscopic crystals, whereas only 7.2 per cent of the specimens in which the p_H was higher than (to the right of) the solubility curve contained microscopic crystals. Of these, one half were voided directly following a specimen that contained gross crystals. It is also significant that in case 1 the urine p_H was lowered and crystalluria occurred when the in vitro solubility was exceeded.

This relationship between the p_H of the urine and the solubility of sulfadiazine is vividly demonstrated by the fact that a specimen containing 788 mg. per hundred cubic centimeters free (60 times the water solubility) and 192 mg. of acetyl sulfadiazine per hundred cubic centimeters (13 times its water solubility) was voided without occurrence of crystals. When the p_H of this specimen was lowered 0.2 p_H unit by addition of a small amount of acid, the clear specimen immediately became milky turbid as crystals of sulfadiazine appeared.

10. Subsequently, with average doses of 4 to 6 Gm. daily the blood cultures became negative.

There are several practical points which may be mentioned. The "routine" use of alkalis will probably not keep the urine alkaline and avoid crystalluria. The quantity of alkali needed should be governed primarily by the p_H of the urine (which should be measured frequently) and not by the amount of sulfadiazine given. Since the morning specimen has the lowest p_H and the highest concentration of sulfadiazine, this seems to be the specimen most apt to contain crystals.[11] Thus, of 22 specimens containing crystals, 17 were morning specimens. For this reason it is advisable to administer alkali at night to counteract this tendency.

Although previous papers have suggested the advisability of adjuvant alkali therapy in patients receiving the sulfonamide compounds, this has not been generally accepted as a method of preventing urinary complications. Two reasons become evident: When used with sulfapyridine, alkalis do not and cannot prevent urinary complications because they do not sufficiently increase the solubility of sulfapyridine and acetyl sulfapyridine within the physiologic range of urinary p_H to prevent renal precipitation. Secondly, with sulfathiazole and sulfadiazine, the usual quantities of alkali given are insufficient to maintain the urine consistently alkaline; in the 2 cases reported here large amounts of bicarbonate were needed to keep the urine at p_H 7.5.[12]

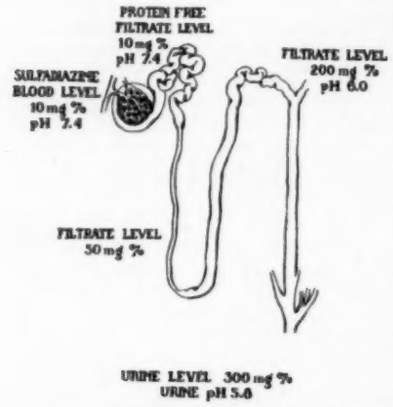

Fig. 6.—Diagrammatic representation of the renal excretion of the sulfonamide compounds. As the urine is formed, the concentration of the sulfonamide may be increased thirty times or more. Precipitation will depend on the solubility of the particular drug at the concentration and p_H resulting from urine formation.

It is important to realize that as these drugs are excreted by the kidney (fig. 6) a concentration of 10 mg. per hundred cubic centimeters in the blood may be increased to 300 mg. per hundred cubic centimeters in the urine as a result of reabsorption of water by the tubules. In addition base is also reabsorbed and the p_H may be lowered from that of the blood (7.4) to as low as 5.5, commonly found in the urine. By thus lowering the p_H in the case of sulfathiazole, sulfadiazine and their acetyl forms, the soluble salts are converted to the relatively insoluble acids, and precipitation takes place. The function of the alkali is to prevent this fall in p_H during the formation of urine.

These studies also suggest a most valuable aid in the lavage therapy of acute or impending renal blockage. Instead of using warm water or warm saline solution in which these drugs are but very slightly soluble, sodium bicarbonate or sodium carbonate solution should be used to dissolve the crystals; the more concentrated the solution, the greater the solvent action.[13]

11. This was also observed during routine therapy with sulfadiazine (Anderson, D., and Rose, H. M.: Unpublished data).

12. Additional alkalis are also needed when sulfadiazine is administered by mouth in the form of the sodium salt. Apparently a large excess of alkali is required to neutralize the usual acidity of the urine. Although the possibility of producing alkalosis and edema might be an objection to the simultaneous use of large amounts of alkali, none was detected in these and numerous other patients to whom similar amounts of alkali were given.

13. It is of interest to note that just recently Wright and Kinsey described large orange yellow crystals in their case 4 which dissolved readily when the urine was alkalized.

SUMMARY

1. There is great variation in the urinary solubility of sulfadiazine, sulfathiazole and their acetyl forms over the physiologic p_H range.

2. Since the solubility of these drugs is greatly increased in alkaline urine, maintenance of a consistently alkaline urine was tried as a means of preventing renal obstruction during sulfadiazine therapy.

3. Two patients with subacute bacterial endocarditis were given massive doses of sulfadiazine, and with certain exceptions their urine was maintained consistently alkaline with large doses of bicarbonate (10 to 20 Gm. daily). No alkalosis or edema resulted.

4. High concentrations of sulfadiazine were held in solution in alkaline urine; oliguria and renal obstruction were prevented. Crystalluria occurred in those urine specimens in which the p_H fell below the in vitro solubility limits.

5. The quantity of bicarbonate to be given should be judged by the p_H of the urine. To maintain sulfadiazine in solution during full therapeutic dosage, a p_H of 7.5 or higher is essential.

6. When alkaline urine is voided with high concentrations of sulfadiazine in solution, decreasing the p_H slightly will immediately precipitate the drug.

7. In the renal (pelves and ureters) lavage therapy of renal obstruction caused by one of the sulfonamide compounds, alkaline bicarbonate or carbonate solutions are recommended, since these will dissolve drug crystals much better than warm water or isotonic solution of sodium chloride. Utilization of this information in routine therapy with sulfathiazole and sulfadiazine in average doses would remove the hazard of their renal complications.

Clinical Notes, Suggestions and New Instruments

ESTIVOAUTUMNAL MALARIA WITH FRONTAL LOBE SYNDROME

MAJOR NORMAN Q. BRILL,
MEDICAL CORPS, ARMY OF THE UNITED STATES
AND
CAPTAIN VICTOR L. PELLICANO,
MEDICAL CORPS, ARMY OF THE UNITED STATES

Since the mobilization program started there has been a shifting of large numbers of men not only within the country but to many points throughout the world. With this wartime flow of population, and with extension of the war to more and more tropical and subtropical countries, the incidence of malaria can be expected to increase steadily.

Many physicians in the armed forces serving in localities far removed from their home have had limited experience with the disease and have had little opportunity to observe the varied fashions in which it may manifest itself. Members of the medical profession in military service must be familiar with the protean manifestations of malaria so that their function to preserve the fighting strength of our forces will not be impaired.

The following case is reported to illustrate that malaria may manifest itself primarily by a syndrome of disease of the frontal lobe of the brain. We have been unable to find a similar case recorded in the literature, though many cases of cerebral malaria have been described.

REPORT OF CASE

W. S., a white soldier aged 24, a native of Texas, had been in the Army for six months serving with an engineer battalion

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when he became ill. On Oct. 15, 1941, during the Carolina maneuvers, he was admitted to an evacuation hospital complaining of severe low backache, pain in the eyes and fever of three days' duration. The patient was dull and confused. He was transferred to the Station Hospital at Fort Bragg, North Carolina, the following day with a diagnosis of influenza and possible encephalitis.

On physical examination the soldier was well developed and well nourished and appeared acutely ill. The skin was flushed and hot. There was no rash. Eye, ear, nose and throat examinations gave negative results except for moderate inflammation of the pharynx. The lungs were clear and the heart was normal. There was no lymphadenopathy. The liver was felt 2 cm. below the right costal margin. The spleen was not palpable. There was a moderate degree of mental confusion and some increase in motor activity, and it was difficult to keep the patient in bed.

Examination of a blood smear on admission showed many parasites of the Plasmodium falciparum type. Blood studies showed 4,210,000 red blood cells per cubic millimeter, hemoglobin 90 per cent and 4,850 white blood cells per cubic millimeter. The differential count was 64 per cent polymorphonuclear leukocytes, 24 per cent lymphocytes and 12 per cent monocytes. Urinalysis was negative.

The patient was treated with atabrine dihydrochloride 1½ grains (0.1 Gm.) three times a day by mouth for five days. A blood smear on October 17 was again positive for Plasmodium falciparum. No parasites were demonstrated in the blood after completion of the course of atabrine. The patient, however, continued to manifest abnormal behavior characterized by increased psychomotor activity, euphoria and slight confusion. He was given quinine 5 grains (0.3 Gm.) three times a day for one week and two doses of plasmochin. By October 30 his mental state had improved somewhat but he complained of generalized malaise and weakness. He was discharged from the hospital to duty on November 8.

On return to his organization he again manifested abnormal behavior and was again referred to the hospital and admitted November 10. The patient complained chiefly of headache and vomiting. The oral temperature was 99.4 F., pulse rate 100 and respiratory rate 20.

On examination he was amenable and cooperative, lying quietly in bed. He was definitely tremulous, with a fairly constant coarse tremor of the extremities on the right side. The patient was unable to give an adequate or coherent story of the events which led up to his hospitalization, though he was oriented in all spheres. There was a decided memory defect, especially for recent events, and some of his replies were irrelevant. He did not recognize one of the physicians who had examined him a half an hour before. He expressed no ideas of reference, no hallucinations and showed no disturbance in affect. Neurologic examination elicited a Babinski sign on the right. The reflexes were slightly less active on the right than on the left side, and the abdominal reflexes on the right were slightly diminished. The red blood cell count was 4,360,000 per cubic millimeter, hemoglobin 90 per cent and the white blood cell count 11,400 with 54 per cent polymorphonuclear leukocytes, 36 per cent lymphocytes, 6 per cent eosinophils and 4 per cent monocytes. Urinalysis was negative. The Kahn reaction of the blood was negative. A blood smear was negative for malarial parasites.

The nature of the illness was not recognized immediately and malarial treatment was not instituted because he was unable to give an adequate history and because he was admitted to a section of the hospital different from the first admission. The following day he was still confused, neurologic signs persisted and the temperature was 102 F. A lumbar puncture was performed on November 12. Spinal fluid was clear and colorless and under normal pressure. There were 64 cells with 40 per cent polymorphonuclear leukocytes and 60 per cent lymphocytes. There was a heavy trace of globulin. Repeated blood smears for malarial parasites were negative. After several days of low grade fever without chills the temperature became normal.

On November 14 neurologic examination revealed a partial, mixed aphasia, alexia and agraphia. He had extreme difficulty in expressing himself, in naming objects and in reading newspaper headlines and was unable to write his name correctly. There was still a definite memory defect for recent events. Babinski and Chaddock signs were elicited on the right and Oppenheim signs and forced grasp reflexes bilaterally, greater on the right than on the left. There was no papilledema or nuchal rigidity. On November 17 he appeared greatly improved. He was more alert and was able to read and write much better. A five day course of atabrine was given as before. On November 22 his mental condition had improved further. A Babinski sign was still present on the right side and the abdominal reflexes were depressed on the left. There was almost complete recovery from the alexia, agraphia and aphasia. On November 25, neurologic examination was negative except for diminished abdominal reflexes and delayed plantar flexion on the right side. He had, however, become definitely euphoric, overproductive and elated and showed a decided increase in his psychomotor activity. He made grandiose plans and was typically hypomanic. Slight difficulty in reading was still present and he would leave out occasional words in writing. By November 30, overactivity had increased to the point at which it became necessary to transfer the patient to the psychiatric ward. He was very distractible and euphoric and stated that he had never felt better in all his life.

A sample of writing addressed to his fiancée during this time is as follows: "Honey, never have I been so happy in all my life. Captain B. is ready to see if we are still going to marry. You did not say one word about it, but honey, I already had another heamonion that I have been having. I have as much sense as anybody now. Boy, that Captain B. has been my very best friend in an hour of kneed. He and I have grown to be very close friends. We want to get that camera and take some of the scenery of all nurses and doctors. Since that night I told those nurses that I could not sleep, I read an article in the paper on a man who never sleeps. He does nothing but sip his old tea. Don't try to forse any man to sleep when a man has the fantastic ideals always and crased ideals of my time that would be one unfortunate moment alive."

In the psychiatric ward he showed gradual improvement; he became less talkative and his judgment improved. As the mental condition improved, he began to complain of malaise, ready fatigue, paresthesias on the left side of the body and pain in the lower extremities. Neurologic examination, however, was unrevealing. By December 26 his memory was good. The pain and paresthesias were less pronounced; he was quiet and cooperative and had developed insight into his mental upset. Improvement continued until Jan. 10, 1942, when he was discharged from the hospital.

His family history and previous personal history were obtained through the assistance of the American Red Cross. The patient's grandparents had died of natural causes at advanced ages and there was no history of mental or nervous disorder in his parents and five siblings.

The patient's birth and early development were normal. He had completed one year of college. His attendance, study habits and behavior were considered perfectly normal. He had never manifested any mental abnormality and had suffered no serious injuries or disease, was not addicted to the use of alcohol and had been considered well adjusted.

COMMENT

The patient's illness began with symptoms which suggested influenza. A blood smear was done shortly after admission to the hospital because the ward officers considered the possibility of malaria. Symptoms of cerebral involvement were manifest almost from the beginning but did not command serious attention and consideration until the second hospital admission, when they dominated the clinical picture.

The fairly rapid response to specific therapy left little doubt concerning the nature of the illness. The manic psychosis which the patient developed is believed to have been secondary

to organic brain disease, especially in view of the completely negative past history of any mental disorder.

It is generally accepted that estivoautumnal malaria is responsible for the major portion of deaths due to uncomplicated malaria and that fatal cases are usually associated with cerebral involvement.[1] In cases in which there is cerebral localization of the parasites, the onset is usually rapid with delirium or coma, and death frequently ensues without a return to consciousness. This is commonly the course in drug addicts who become directly inoculated with infected blood.[2] Many different types of atypical malarias with symptoms in the nervous system have been described.[3] They have been classified as (1) meningitic type, (2) monoplegic or hemiplegic type, (3) myelitic type, (4) ataxic type, (5) disseminated sclerotic type, (6) bulbar type, (7) cerebellar type, (8) cerebral type, (9) polyneuritic type, (10) Korsakoff type and (11) aphasic type.

The classification indicates that the disease may involve any part of the nervous system and resemble many different disease entities. The symptoms produced depend on the anatomic localization of the disease.

In fatal cases, the brain shows a gross brownish discoloration of the gray matter with macroscopic punctate hemorrhages into the white matter. Stained sections reveal the capillaries filled with parasites in various stages of development.[1]

In the present case, observations indicate that the predominant involvement was in the frontal lobes. The picture is one of rather diffuse organic brain disease complicated by the development of an organic psychosis and terminating with recovery.

SUMMARY

A puzzling case of organic disease of the brain, manifested by aphasia, alexia, agraphia, memory defect and confusion associated with involvement of the pyramidal tracts and bilateral forced grasp reflexes and complicated by an organic psychosis proved to be one of cerebral malaria. Cure was effected by the early administration of atabrine.

1. Coggeshall, L. T.: Malaria, in Cecil, R. L.: A Textbook of Medicine, Philadelphia, W. B. Saunders Company.
2. Helpern, Milton: Malaria Among Drug Addicts in New York City, Pub. Health Rep. **49**: 421 (March 30) 1934.
3. Castellani, Aldo, and Chalmers, A. M.: Manual of Tropical Medicine, New York, William Wood & Co., 1919.

From the Department of Medicine, Duke University School of Medicine.

TWO CLINICALLY USEFUL SIGNS

1. THE WHISTLE-SMILE REFLEX IN THE PARKINSONIAN SYNDROME
2. THE 'NEPHRITIC STARE' IN CHRONIC NEPHRITIS

FREDERIC M. HANES, M.D.
Florence McAlister Professor of Medicine, Duke University School of Medicine
DURHAM, N. C.

1. When the normal individual is requested to whistle he does so and then smiles, probably as a mimetic response to the absurdity of unmotivated whistling. The patient suffering from the parkinsonian syndrome does not smile after whistling. For many years I have employed this simple test as an aid to rapid orientation and have found it to be very helpful and reliable.

2. While I was serving as a house officer at Johns Hopkins Hospital in 1909 a patient was admitted in a suburemic state, showing definite exophthalmos.[1] Under treatment she improved and concomitantly the proptosis became less pronounced. After some months she was readmitted and died in uremia. An autopsy confirmed the clinical diagnosis of chronic glomerulonephritis. The thyroid was normal.

Thirty years' experience with the eye signs of Bright's disease, which are similar in every way to those seen in toxic goiter, has proved that they are frequently useful in differentiating cardiac breakdowns as a result of chronic kidney disease from those due to other causes. Cardiac or cerebrovascular syndromes frequently mask the basic renal background in chronic glomerulonephritis, nephrosclerosis, necrotizing arteriolitis and pyelonephritis until the onset of renal decompensation.

1. Barker, L. F., and Hanes, F. M.: Exophthalmos and Other Eye Signs in Chronic Nephritis, Am. J. M. Sc. **138**: 469, 1909.

The "nephritic stare" does not serve to differentiate various types of nephritis. My assistant Dr. Joseph Stevens studied in this clinic 100 instances of chronic Bright's disease, with especial reference to eye signs. Forty-three of these showed the "nephritic stare," some with varying degrees of proptosis,

Fig. 1.—The nephritic stare in a patient with chronic glomerulonephritis.

as measured by the ophthalmometer. Thirty of these patients came to autopsy, with the following anatomic diagnoses:

Chronic glomerulonephritis with "nephritic stare" and proptosis 16.

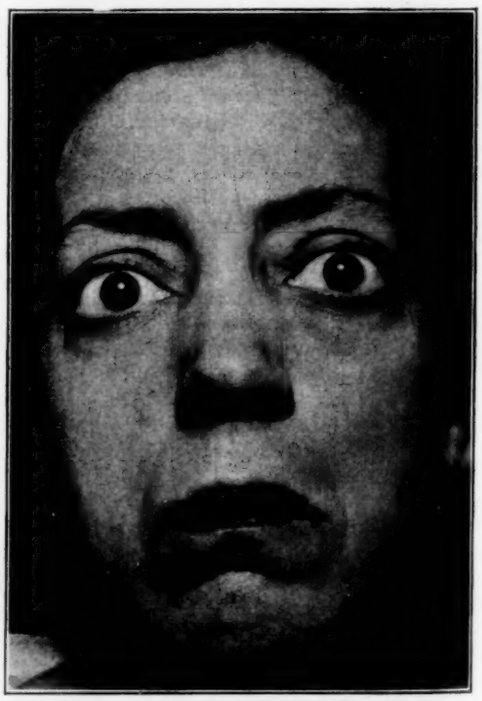

Fig. 2.—Exophthalmos in a patient with chronic glomerulonephritis proved by autopsy.

Chronic glomerulonephritis with "nephritic stare" and no proptosis 0.

Arteriosclerotic nephritis with "nephritic stare" and proptosis 7.

Arteriosclerotic nephritis with "nephritic stare" and no proptosis 5.

Pyelonephritis with "nephritic stare" and no proptosis 2.

Negro patients 14, white patients 16.

Although I have used the term "exophthalmos" it is more correct to refer to the sign as the "nephritic stare" (fig. 1), for proptosis is, as a rule, not measurably present, even when the fixed stare is clinically obvious. The stare is indistinguishable from that often seen in early toxic goiter, from which, of course, it must be differentiated. On the other hand, Plummer and Wilder [2] are in error when they say that the clinical impression of proptosis in such patients is very seldom confirmed by exact measurements with the exophthalmometer. A measurable grade of exophthalmos is not rare (fig. 2), though the "nephritic stare" may be clearly discernible in the absence of proptosis.

The factor that leads to the characteristic appearance of the "nephritic stare," exclusive of actual proptosis, is retraction of the upper lid (Dalrymple's sign). This lid retraction may produce the appearance of exophthalmos when no proptosis is actually present.

Council on Industrial Health

THE COUNCIL ON INDUSTRIAL HEALTH HAS APPROVED PUBLICATION OF THE FOLLOWING SPECIAL WARNING BULLETIN ON EPIDEMIC KERATOCONJUNCTIVITIS.

C. M. PETERSON, M.D., Secretary.

EPIDEMIC KERATOCONJUNCTIVITIS

This report is issued jointly by the U. S. Public Health Service and the Committee on Industrial Ophthalmology of the Section on Ophthalmology, American Medical Association. It is recognized that relatively few cases of epidemic keratoconjunctivitis will be reported in areas which are not essentially industrial, but the condition has appeared so extensively throughout the country that the agencies sponsoring this report hope that physicians everywhere will be prepared to apply the recommendations listed below promptly and effectively.

INCUBATION PERIOD

The incubation period in epidemic keratoconjunctivitis ranges from five to ten days.

CLINICAL MANIFESTATIONS

The onset may be preceded by a low fever and mild generalized malaise. The local ocular symptoms are merely those of a foreign body or conjunctival irritation. One eye is usually affected first, and in a large percentage of cases the second eye becomes infected within five to eight days. Preauricular and submaxillary glandular involvement with tenderness is common in a high percentage of cases.

Edema of the lids and the conjunctiva, especially the transitional fold, is very frequent. The conjunctiva presents the appearance of a simple purulent conjunctivitis but with little or no formation of pus. Small areas of pseudomembrane are not infrequent and, when removed, leave either small white dotted points or some bleeding points. The bulbar conjunctiva becomes edematous early. At this stage there is some lacrimation and photophobia, but real pain and blepharospasm do not appear until the cornea becomes involved.

The proportion of cases in which corneal involvement occurs varies from 50 per cent to 90 per cent. In six to twelve days after the conjunctivitis appears, the cornea becomes involved by the appearance of discrete gray infiltrates that lie in and immediately under the epithelial layer of the cornea. They may be confined to the periphery of the cornea but in a large percentage of cases involve the pupillary area of the cornea directly. These infiltrates are discrete and seldom become complicated by an erosion of the corneal epithelium with resultant staining with fluorescein. The extent of visual impairment depends on the number of infiltrates and their location.

2. Plummer, W. A., and Wilder, R. M.: Etiology of Exophthalmos, Arch. Ophth. **13**: 835 (May) 1935.

CLINICAL COURSE

The disease is self limited. In the majority of instances the conjunctivitis disappears spontaneously in fourteen to eighteen days. The corneal complication may disappear in seven days or may last for many months. The longer they persist the greater is the danger of permanent visual impairment.

LABORATORY FINDINGS

Scrapings of the conjunctiva show a preponderance of monocytes. Cultures and smears either are negative or show the usual contaminations.

TREATMENT

There is no specific treatment that has shown a definite influence on the course of the disease. During the acute stage the eyes should be kept clean with irrigations of boric acid, isotonic solution of sodium chloride or 1:5,000 mercuric oxycyanide. If there is much photophobia, 1 per cent holocaine may be instilled at frequent intervals. Five per cent sulfathiazole ointment has been used, as has 5 per cent solution of sodium sulfathiazole sesquihydrate. For persistent corneal infiltrates, the x-rays have seemingly yielded some results.

PERIOD OF INFECTIVITY

It is not yet known how long the danger of transmission to others exists. At present for practical purposes a sufferer from epidemic keratoconjunctivitis may be allowed to return to work when the active conjunctivitis has disappeared.

PREVENTIVE MEASURES

At present the only preventive measure known is complete isolation of infected persons. As the disease has been transmitted through medical personnel, the most meticulous asepsis must be insisted on. Not only must physicians and nurses wash their hands thoroughly with soap and water after each patient, but also eye droppers, solutions and instruments must be sterilized to prevent infection of noncontaminated persons. The infected individual must be told of the danger of transmission of this disease to others, not only in the plant, but even in the home surroundings. It is suggested that in industrial plants where epidemic keratoconjunctivitis has made its appearance the following methods of procedure be adopted:

1. In smaller plants with a limited personnel, every individual with a red eye should be stopped at the entrance of the plant and sent direct to the plant physician to determine whether or not epidemic keratoconjunctivitis is present. In larger plants where such a procedure is not possible, supervisors and foremen should be instructed in detail to make rounds immediately when a fresh shift starts and send any individual with a red eye to the medical office.

2. If the cases are to be treated at the medical department of the plant, a separate room should be set aside for such cases and in that room there must be exercised the most scrupulous asepsis, even to washing the arms of the chairs in which the patients sit. Aside from the aseptic and separate care of the recognized cases of the disease, special cleanliness of the hands of the physician in the general clinic should be maintained, with the use of an effective disinfectant between cases lest the infection be spread by means of undiagnosed cases, especially those suspected of having foreign bodies in the eye.

3. Every case of epidemic keratoconjunctivitis should be excluded from the communal facilities of the plant until the inflammation has subsided to the point where the plant physician considers it no longer transmissible.

4. Explicit instructions should be given to every individual regarding the danger of transmission and emphasizing the decrease in the war effort as a result of the time lost from epidemic keratoconjunctivitis.

5. The local health authorities should be notified immediately of the existence of individual cases.

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SATURDAY, APRIL 3, 1943

NEUROPSYCHIATRY IN THE ARMY

Under Medicine and the War in this week's issue of THE JOURNAL appears a brief report of the establishment of a special school for neuropsychiatry under the auspices of the United States Army Medical Corps. Psychiatric problems represent today some of the most important of those that confront our armed forces. In 1918 there were 7 men of each thousand discharged for psychiatric reasons, whereas in 1942 the rate was 4 per thousand. At the time of induction in 1918 only 20 men of each thousand were discharged for psychiatric reasons; now about 75 of each thousand are rejected for such causes. This does not mean that more men are now mentally unfit; our scientific methods have improved sufficiently in the interval to enable more accurate detection of such cases. The indications are that 30 per cent of the casualties now arriving from the war zones are psychiatric in character or have some well defined psychiatric aspects. Nervous and mental disorders are major causes of medical discharge from the Army. Conceivably the technic developed for induction, including the filtering by the local draft boards and the induction boards, has not been sufficient to prevent entrance into the service of a large number of unstable persons. The service in this respect is improving, but, unless the deficiencies are fully recognized, those who are striving for this improvement may be handicapped and delayed in accomplishing a satisfactory result.

The detection of the mentally unsuited or the potential psychiatric casualty at induction is one of the most important tasks of military neuropsychiatry. The lack of sufficiently trained examiners, the lack of technic for securing necessary historical information about inductees, the large numbers inducted and the short period of time during which induction occurred are all contributory factors in the failure to control properly the admission of those not mentally qualified. The fault cannot be credited to any single agency. Everything possible was done by Selective Service headquarters and by cooperative efforts between the armed forces and Selective Service. No doubt the training of many more men in the special problems of psychiatry related to the armed forces will help this situation.

The need for special consideration of neuropsychiatric problems was recognized early after our entrance into the war with the establishment of a committee for this purpose in the Division of Medical Sciences of the National Research Council. In February 1942 a Neuropsychiatry Branch was established in the Surgeon General's Office under Lieut. Col. Patrick S. Madigan, who had many years of experience in this specialty in the Regular Army. As the problem grew and became more definitely recognized an assistant chief, Lieut. Col. Malcolm J. Farrell, was appointed in April 1942. Then in August 1942 Col. Roy D. Halloran was assigned to duty as chief of this branch. Among the most important duties of the branch are (1) giving advice to the Surgeon General and other governmental agencies on neuropsychiatric matters, (2) recommending policies for the Army in neuropsychiatric matters, (3) inspecting neuropsychiatric facilities in hospitals and clinics, (4) making recommendations for circular letters and directives regarding neuropsychiatric matters, (5) reviewing neuropsychiatric information coming into this office, (6) maintaining a card index of location and qualifications of neuropsychiatric officers, (7) consulting with the personnel division and recommending assignments and transfers of neuropsychiatric officers, (8) reviewing and approving scientific publications submitted by neuropsychiatric officers and (9) attending and participating in National Research Council meetings.

As this section of the Surgeon General's Office became oriented in its responsibilities, consultants were appointed to coordinate and supervise clinical and administrative neuropsychiatry. Thus far four consultants have been appointed: Lieut. Col. Franklin G. Ebaugh, M. C., to the eighth service command, Lieut. Col. William C. Menninger, M. C., to the fourth, Major Garland H. Pace, M. C., to the seventh and Lieut. Col. Douglas A. Thom, M. C., to the second. In the European theater of operations Lieut. Col. Lloyd J. Thompson acts as consultant in neuropsychiatry and in the Southwest Pacific theater of operations Lieut. Col. Samuel A. Challman.

Most important in this service has been the establishment of the School of Military Neuropsychiatry, which has already been mentioned. More than a hundred and twenty officers have already been trained in this course. A neuropsychiatric unit at the Thirty-Sixth Station Hospital has been organized under the command of Lieut. Col. Ernest H. Parsons. This unit is functioning as a neuropsychiatric center in the European theater

and is providing indoctrination instruction for newly arrived neuropsychiatric officers so that they may familiarize themselves quickly with the problems and case material. Especially qualified trained psychiatrists have been assigned to carry out planned mental hygiene programs at replacement training centers.

The question of morale is being met by liaison established between the Neuropsychiatric Branch, represented by Lieut. John Appel, and the Special Services Branch of the Army, which is under the direction of Gen. Fred Osborn.

Finally, neuropsychiatry in the armed forces must be especially concerned with problems of delinquency. The crude methods of the past have given way to more humane and satisfactory handling of the problems of the homosexual. No longer is it necessary to subject cases that are so definitely in the medical field to the routine of military court martial.

The development of the Neuropsychiatric Branch of the United States Army Medical Department represents one of the most important achievements in the advancement of military medical science. All of those officially responsible merit commendation for their cooperation in the significant results that have already been secured.

EXTENSION OF PUBLIC HEALTH COVERAGE TO THE NATION

Forty million of our people live in communities or in areas in which there is no access to the full time services of a professionally trained medical officer of health and the associated sanitarians and public health nurses of a local health department of civil government. On June 10, 1942 the House of Delegates of the American Medical Association unanimously voted its approval of extension of such services. Now the Committee on Administrative Practice, one of the standing committees of the American Public Health Association, has offered a plan to improve the situation.

Tax supported public health services have been distributed unevenly and not in all respects in relation to sanitary needs or in proportion to the population units of local government. In fact, there are conditions of local government, cities, townships and counties, in which duplicating and to some extent conflicting health services are provided because of local rivalries of a political nature. State laws in some instances do not authorize cooperative arrangements for a single health officer for adjacent communities or counties. Good health service for prevention of communicable, occupational, nutritional and other preventable diseases, and for the protection of the health of mothers and children, cannot be achieved for a state solely or effectively or economically by a state department of health unless the counties and cities are sufficiently concerned with local health conditions to support their own community health services. By the same token federal programs for a higher level of national health fail in effectiveness for lack of facilities of local government through which federal grants can be used by agreement with the state.

In July 1942 some 62 million people living in the continental United States were provided by local governments with full time medically officered health protection. In addition 16½ million persons were served by county or district health departments operated by a state department of health, and about 12 million more people living in cities with full time health services. There remain 41,052,600 persons, or 31 per cent of our population, in 1,687 counties in 41 states for whom no full time health service is provided by either local or state government.

The committee of the American Public Health Association presents a half dozen basic principles of health administration and suggests that not more than 1,127 units of local health jurisdiction are needed for the total coverage of the continental United States. The units are, of course, in addition to the respective state departments of health and the health services of the various bureaus and departments of the federal government. It is to be assumed that a city and the county within which it is located shall have a single headed health service. It is suggested that a unit of less than 50,000 population can rarely maintain an efficient tax supported local health service and that counties with small populations should be authorized by state law to combine with adjacent counties to support and be served by a single district or multicounty health department.

Among the 3,070 counties of our states there are many with populations so small and economic resources so slender as to preclude the possibility of supporting even the minimum personnel and functions of a local health department. The basic public health law of each state should not only permit but specifically authorize the creation of local health units of population size and area compatible with efficient and economical public service. The law should provide furthermore for the selection of professional personnel on a sound civil service or merit system and authorize the levying of taxes to support the health services.

The American Public Health Association, through its Subcommittee on State Health Administration, has recently completed a study of state health administration in Illinois, undertaken at the request of the state director of public health with the approval of the governor. A summarized report of this study discloses a recommendation that legislation be enacted to permit the establishment of full time county or combination of county health departments. Following a distribution of this report, the Research Department of the Illinois Legislative Council made available a factual study of

county health departments in the state for use by the general assembly in considering any legislation that might be proposed. Now a bill has been introduced by Senator Searcy, as S. 244, authorizing the establishment and maintenance of county and multiple county health departments in the state.

Permissive in form, this legislation proposes that county full time health departments may be created either by resolution of a county board or by the voters of a county and that multiple county health departments may be set up. If four or more counties wish to associate themselves in establishing and maintaining such a department, prior approval must be obtained from the state department of public health. Provision is made for the levying of a special tax not to exceed 1 mill on the dollar on all taxable property in the county or counties involved to finance the operation of the department. Existing full time health departments in cities, villages or public health districts with less than 500,000 inhabitants may be retained or they may be abandoned and become integrated in the county or multiple county health department. Health departments in communities with a population of 500,000 or over will apparently not be affected by the bill. Each county health department will be managed by a board of health appointed by the president or chairman of the county board. At least two members must be physicians licensed in Illinois to practice the healing art in all its branches and at least one member must be a dentist licensed in Illinois. All members must be chosen for their special fitness for membership on the board. Multiple health departments are to be managed by a board of health consisting of three members appointed from each county by the president or chairman of the county board.

Provision is made for the appointment of medical, dental and nonmedical advisory committees and for the appointment, for each department, of a chief medical officer to act as executive officer, and of such other officers and employees as may be approved by the executive officer, all appointees to meet the qualifications prescribed by the Illinois State Civil Service Commission. The functions to be exercised by the departments are set forth in broad groupings, including the right to pass such rules as may be necessary for the improvement and protection of the public health. The people of Illinois may well reflect on the importance of this proposal, establishing as it does a framework on which may be constructed a comprehensive public health program to function in the interest of the health of all the people of the state. Legislation with a similar objective, although differing in detail and approach, was proposed this year in the states of Arkansas, Georgia, North Dakota, Utah, Washington and Wyoming.

Each state medical society may with advantage avail itself of the detailed information in the hands of the American Public Health Association and analyze its own situation in conference with its own state health officer. Permissive or enabling legislation to provide for local health units and their support should be supported by the professional influence of the physicians of the state, unless existing laws are adequate.

The career of public health as a specialty of medicine requiring graduate university training and practical experience is so far accepted as part of the pattern of preventive medicine that the survival of the part time general practitioner as the local administrator of a health department cannot be encouraged by the medical profession or be recommended to the taxpayer as the best his money can buy in public health.

FOOD POISONING

During the present mobilization the incidence of food poisoning in U. S. Army troops is much less than that being experienced by other armed forces engaged in the present conflict. However, many food poisoning outbreaks are due to (1) carelessness in the handling of sanitation involved in the processing or serving of food and (2) the presence of unrecognized human carriers of enteric pathogens in the permanent food handler group.

The Army has focused the attention of medical officers and personnel involved in the operation of all messes on the necessity of protecting food adequately from contamination by processing and serving under sanitary conditions and by preventing undue retention of food that may be potentially contaminated prior to its being served. Laboratory facilities have been made available for the investigation of these outbreaks when they occur, and every effort is being made to determine their source.

In general, food as delivered by the manufacturer or wholesaler for processing in army kitchens has not been found to be an important factor in the cause of these outbreaks. Most of the outbreaks that have occurred have been due to the fact that foods such as potato salad, ground meat and sliced ham have been processed too long in advance of serving or have been stored under conditions favoring bacterial growth. Those outbreaks that have not been satisfactorily worked out with regard to the cause and the source of infection have in many instances been due to the fact that personnel involved have been convinced that physical factors or bacteria such as the staphylococcus were the only agents involved in the outbreak. Staphylococcus food poisoning does occur, and this type of infection is important as an etiologic agent of food poisoning. However, when mediocre bacteriology is done in con-

nection with the investigation of the outbreaks the individuals conducting the investigation usually isolate a coccus which by gross methods of examination is identified as a staphylococcus. This finding, in conjunction with perfunctory examination for the Shigella and Salmonella organisms, leads to the conclusion that the outbreak is essentially staphylococcic in origin. These conclusions are not justified in many instances. The findings of more thorough examinations definitely proved that the outbreak itself was not due to staphylococci but to Shigella or Salmonella.

The detection of permanent food handling carriers of Shigella or Salmonella and their removal from this type of work definitely limit the possibilities of subsequent outbreaks. If the examination of the outbreak is perfunctory and staphylococci are blamed for the outbreak without adequate investigation for other possible organisms, corrective action will not be taken and the outbreaks will continue to occur. Medical schools and other scientific organizations should bring to the attention of physicians the necessity for insisting on thorough investigations of food poisoning outbreaks and not accept perfunctory explanations with regard to their cause.

Current Comment

INVALID DIETS AND FOOD RATIONING

Physicians who are especially concerned with diets for invalids should note that ration order 13, issued by the Office of Price Administration under date of Feb. 9, 1943, covering all canned, dried and frozen fruits and vegetables, permits under article II, section 2.5, extra rations for invalids. The order reads:

> Consumers who need more processed foods because of illness may apply for more points. (*a*) Any consumer whose health requires that he have more processed foods than he can get with War Ration Book Two may apply for additional points. The application must be made, on OPA Form R-315, by the consumer himself or by some one acting for him and may be made in person or by mail. The application can be made only to the board for the place where the consumer lives. He must submit with his application a written statement of a licensed or registered physician or surgeon showing why he must have more processed foods, the amounts and types he needs during the next two months and why he cannot use unrationed foods instead.
>
> (*b*) If the board finds that his health depends on his getting more processed foods and that he cannot use or cannot get unrationed foods, it shall issue to him one or more certificates for the number of points necessary to get the additional processed foods he needs during the next two months.

The application form referred to, OPA Form R-315, is apt to be somewhat confusing to patients. It is titled "Sugar Special Purpose Application" and was developed primarily to meet the need for home canning. It is being used temporarily, until a more adequate form can be developed. The procedure indicated in section 2.5 may be changed somewhat in the future, in which case due notice is to be provided.

THERAPY OF SEVERE BURNS

Generally it is believed that severely burned patients should be kept warm because of the fall in body temperature commonly accompanying shock. This conventional belief is now challenged by Elman and his co-workers [1] of the Department of Surgery, Washington University School of Medicine, St. Louis, as a result of their study of the effects of different environmental temperatures on the mortality rate of severely burned laboratory animals. In the course of a study of chemical changes following severe burns, the St. Louis surgeons noted an increased mortality of their experimental animals during several hot days of the summer when the environmental temperature rose to 95 F. The suggested deleterious effect of such high temperatures was tested on groups of rats placed after burning in rooms at different constant temperatures. Summarizing their experimental data, Elman concludes that the least mortality occurs at an environmental temperature of 75 F., increasing to a 100 per cent mortality with either an increase or a decrease of 20 degrees F. from that therapeutic optimum. Their most favorable temperature (75 F.) is but slightly higher than the level accorded to be the normal average for human comfort. The St. Louis surgeons conclude that "the commonly used heat tent which increases the environmental temperature above that point will be deleterious by increasing the mortality in severe burns" and that the room temperature should be lowered for burned patients in climatic extremes where the environmental temperature rises much above 75 F.

TETANUS IN THE MIDDLE EAST

In the British army each man is inoculated with two doses of 1 cc. of tetanus toxoid at an interval of six weeks. A "boosting" third dose is given not earlier than six months later. Although the procedure is voluntary, probably over 95 per cent of the soldiers, according to Boyd and MacLennan,[1] are inoculated. Only recently have a large percentage received the third dose. Each wounded man is given a dose of 3,000 international units of tetanus antitoxin. Further weekly doses of the antitoxin are given to the patients who have not been actively immunized. Despite the relative rarity of tetanus bacilli in soil samples of the Middle East (8.8 per cent of ninety-one samples of earth collected between Daba and Benghazi) the organisms are not uncommonly found in wounds. In a series of 214 wounds of a severe type, Clostridium tetani was found in 18 (8.4 per cent). During the first two years of war in the Middle East 18 cases of tetanus were reported in the fighting forces. Of these 13 were in the nonimmunized group, while 5 occurred among the actively immunized. The former group had six fatalities and the latter three. From these figures active immunization, while effective in preventive tetanus, apparently has definite limitations. The authors emphasize that 1 of the 3 who died did not have his third dose, while the other 2 in all probability succumbed to an overwhelming infection resulting from masses of

1. Elman, Robert; Cox, W. M., Jr.; Lischer, C. E., and Mueller, A. J.: Proc. Soc. Exper. Biol. & Med. **51**: 350 (Dec.) 1942.
1. Boyd, J. S. K., and MacLennan, J. D.: Tetanus in the Middle East: Effects of Active Immunization, Lancet **2**: 745 (Dec. 26) 1942.

necrotic tissue in their wounds. Boyd and MacLennan stress therefore the necessity of careful surgical treatment with removal of all dead tissue as an important factor in preventing the development of tetanus. The importance of the third, the "boosting," dose of the toxoid, because of its augmenting effect on antitoxin production, is generally accepted.

THE SUPPLY OF PHYSICIANS

Elsewhere in this issue (p. 1160) appears a report released by the Office of War Information concerning the supply of physicians in the United States at this time. Significant is the opinion of the governmental agency that the health of the nation as a whole has not been seriously impaired by any shortage of doctors, that the number of communities critically in need of doctors is not great compared with the total number of communities in the country, and that it might have been better if there had been from the first an agency capable of protecting the needs of the civilian population in the recruitment of doctors. Thus far the relocation of physicians has not wholly solved the problems that prevail. The situation is not now out of control, but luxury medicine is out for the duration. Evidence is not available as to the nature of the personnel utilized by the Office of War Information in making this survey or as to the technic used by the surveyors in securing information. Apparently the investigators failed to utilize fully the facts and data of the Procurement and Assignment Service. For example, the figures of percentage attainment of quotas on Dec. 1, 1942 are at variance with those tabulated by the Procurement and Assignment Service from the Adjutant General of the U. S. Army and the Surgeon General of the U. S. Navy. Frequently throughout the release, isolated or remote communities are cited with low physician population ratios and given as evidence of the breakdown of Procurement and Assignment Service. Upon closer inspection it becomes evident that many of these communities did not have more favorable ratios prior to the war. Rather too great emphasis seems to have been placed on a statement from one county medical society in a Southern state which was certainly not typical of the vast majority of medical societies in this country. Moreover, the investigators seem to have been a little naive in accepting such statements as that of the physician who is said to have slept only three hours a night for a considerable period. The report will, of course, come to the attention of the Procurement and Assignment Service for Physicians, Dentists and Veterinarians, which is the governmental agency charged with the problem of supplying physicians for the armed forces, industry and the civilian population. As a branch of the War Manpower Commission, with which also is associated the Selective Service System, there seems to be no reason why this agency should not be able to meet needs as they develop, keeping in mind always, however, the fact that the first problem of the nation is the winning of the war and that it is the duty of civilians in wartime to sacrifice largely in maintaining the armed forces at the utmost peak of health and physical fitness.

THE INCREASING INCIDENCE OF BACILLARY DYSENTERY

Recently Silverman and Friedrichs [1] reported a study of some 700 bacteriologically proved cases of bacillary dysentery or Bacterium dysenteriae infection of the bowel. The latter term is reserved by the authors for cases of chronic infection with the bacillus of dysentery in the absence of diarrhea or the classic syndrome of dysentery. The responsible organism in the cases of dysentery observed by Silverman in a previous report was Bacterium flexneri. At a later period the predominant organism was found to be the lactose fermenter of Duval. At present the cases show increased virulence and more frequent incidence of complications, the predominant strains being those of Bacterium shigae and of B. flexneri. Although these observations are confined to the New Orleans area the disease shows a definite tendency, as predicted by Silverman in an earlier report (1926), to become endemic in many states of the Union. This prophecy has been borne out by the reports of cases from the states of New York, New Jersey, Illinois, California, Vermont, Missouri and Virginia. The authors advance the concept that arthritis, myocarditis, vascular dysfunction and even obstructing spasm of the colon as seen in chronic dysentery are probably manifestations of protein hypersensitiveness to the bacillary dysentery infecting the patient. Silverman treats such manifestations as allergy by desensitization of the patient with autogenous vaccine. It has not been generally appreciated that these infections may cause deeply penetrating lesions in the bowel with consequent perforation. A person with bacillary dysentery infection of the bowel in a period of remission, following treatment or without treatment, is always a potential victim of this most serious complication. The problem posed by the increase in incidence of bacillary dysentery is pertinent to the aggregation of great numbers of men in the different camps and various communities. The authors believe that the possibility of the spread of this infection from a local community to one of the camps is great. Close vigilance should be observed; should dysentery appear, the patient should be isolated and every effort be made to prevent the spread of the disease.

NEW JOURNAL OF GASTROENTEROLOGY

The council and members of the American Gastroenterological Association have felt the need of a journal with editorial and advertising policies directly under their control. The first issue of the new journal under these auspices, entitled *Gastroenterology*,[1] has now appeared. It contains articles by a number of specialists in the field of gastroenterology. A further list of interesting articles is scheduled for appearance in later issues. As pointed out by Dr. W. C. Alvarez, the editor, the success of the journal now will depend on the degree of interest shown in it by those physicians who are concerned with the advancement of gastroenterology.

1. Silverman, D. N., and Friedrichs, A. V.: The Increasing Incidence and Complications of Chronic Bacillary Dysentery, New Orleans M. & S. J. **95**: 401 (March) 1943.

1. Gastroenterology, official journal of the American Gastroenterological Association, Williams & Wilkins Company, Mount Royal and Guilford avenues, Baltimore.

MEDICINE AND THE WAR

In this section of The Journal each week will appear official notices by the Committee on War Participation of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medicine and the war and such other information and announcements as will be useful to the medical profession.

ARMY

SCHOOL OF MILITARY NEUROPSYCHIATRY

COLONEL ROY D. HALLORAN
Medical Corps, Army of the United States
AND
LIEUT. COL. MALCOLM J. FARRELL
Medical Corps, Army of the United States

The Neuropsychiatric Branch of the Surgeon General's Office announces the opening of a School of Military Neuropsychiatry at the Lawson General Hospital, Atlanta, Ga. The clinical and administrative practice of military neuropsychiatry presents many new and difficult problems to the newly commissioned neuropsychiatrist. The civilian professional experience of neuropsychiatrists varies considerably: psychoanalysts, neurologists, state hospitals, prison psychiatry, child guidance and similar specialties. On entering the Army they are faced with common problems such as the selection and detection of mental misfits, the necessity for short periods of observation, puzzling and bizarre clinical manifestations peculiar to the military service, and the administrative machinery set up to provide for the disposition of neuropsychiatric cases. It has been necessary, therefore, to provide some means whereby the practice of neuropsychiatry in the Army could be made more standard and uniform, to provide the individual officer with an opportunity to review subjects which he did not require in civilian life and to introduce him to the various administrative procedures which will bewilder him if no assistance is provided.

In recognition of these difficulties and to prepare the officer better for the handling of combat casualties, the School of Military Neuropsychiatry, which is unique in Army history and has already gained international attention, was developed with the active interest and support of Major Gen. James C. Magee, the Surgeon General, and Brig. Gen. Charles C. Hillman, Chief, Professional Services, Office of the Surgeon General, to provide practical instruction for already trained and qualified specialists.

Brig. Gen. William C. Sheep, the commanding general of Lawson General Hospital, a well known military neuropsychiatrist, is commandant; the assistant commandant is Col. William C. Porter, also a prominent military neuropsychiatrist, who is in direct charge of the school. Colonel Porter teaches the military aspects of neuropsychiatry, based on his broad experience. Dynamic psychiatry, from a military point of view, is taught by Lieut. Col. M. Ralph Kaufman, and psychiatry from an organic point of view is taught by Major Joseph L. Fetterman. Neurology is taught by Major William H. Everts. Lectures on other related subjects are given by specially selected officers, while certain members of the class relate special experiences such as neuropsychiatry in the Air Corps, Tank Destroyer, Ranger and other special training camps. While these subjects are covered by some didactic lectures, much time is devoted to seminars and round table conferences. Clinical material of a type obtainable only in Army hospitals is provided, since experience has shown that the best method of teaching military neuropsychiatry is by constant reference to and the use of military casualties. In this manner the military administrative considerations which have presented or may present difficulties are thoroughly discussed. Thus the various aspects of military neuropsychiatry which confront the new officer and present difficulties to the older officers are well coordinated by excellent and experienced teachers. The advantages of mutual exchanges of experiences and opinions in the interest of uniformity and professional progress cannot be overestimated.

The quota of officers selected for each intensive four weeks' course, which began Jan. 2, 1943, include officers from each service command and the Air Corps, together with newly commissioned officers from training pools in general hospitals. In this manner new officers have the advantage of the experience of older officers and the older officers have, in turn, the opportunity of evaluating their experiences and methods in the light of experiences and methods of others. Here is demonstrated the adaptation of clinical teaching, the bedside method, to the field of military neuropsychiatry.

PSYCHIATRIC OUTPATIENT DEPARTMENT AT MITCHEL FIELD

The "outpatient" department of psychiatry at Mitchel Field, N. Y., where soldiers with emotional and mental problems may receive advice and treatment without hospitalization, was established five months ago. Among 100 soldiers who have consulted the medical officers, many have been helped to make the transition from civilian to military life and to ease over emotional barriers that might have become serious. The chief of the Neuropsychiatric Service at Mitchel Field is Major Benjamin H. Balser, who directs the outpatient department in addition to the regular ward for mental cases, both under the general supervision of Lieut. Col. Oliver K. Niess, surgeon of Mitchel Field. On the neuropsychiatric staff are First Lieut. William L. Fearing of the Medical Corps and Second Lieut. Margaret L. E. Kram of the Army Nurse Corps. All the officers have had extensive training and experience in neurology and psychiatry. The provost marshal refers certain soldier prisoners to the clinic, taking into account the possibility of mental illness as a basis for misbehavior, and seeks a recommendation from the psychiatrist. In many cases the punishment will be qualified accordingly. The psychiatrist is frequently called on to testify at courts-martial involving such prisoners.

MEDICAL OFFICERS PROMOTED TO BRIGADIER GENERALS

In an announcement sent from the White House on March 25 it is stated that the President recommended to the Senate the promotion of the following medical officers from the rank of colonel to brigadier general (temporary):

Col. George F. Lull, now in charge of personnel in the Office of the Surgeon General.
Col. James S. Simmons, epidemiologist.
Col. Norman T. Kirk, commanding officer of the Percy Jones General Hospital, Battle Creek, Mich.
Col. Leon A. Fox, recently assigned to the special commission on typhus fever.

Brig. Gen. Norman T. Kirk, commanding officer of the Percy Jones General Hospital, Battle Creek, Mich., has been designated by the Surgeon General as chief consultant in orthopedic surgery. This is in addition to his duties as commanding officer of the Percy Jones General Hospital. In his service as consultant he will not be dislocated from his present station.

OFFICE OF WAR INFORMATION

THE SUPPLY OF PHYSICIANS

An Official Release from the Office of War Information

Approximately one third of the doctors in active full time practice in the United States have now been called to the colors. The Office of War Information has just completed a survey to determine the effect on the civilian population of this extensive depletion of the number of physicians and surgeons in private practice.

Between 40,000 and 45,000 doctors have entered the armed services. As the size of the Army and Navy increases, more will be called. The men in the uniform of the United States have been and will continue to be the best cared for medically in the world. But in total war the health and working power of the civilian is as important as the health and striking power of the fighter. The available supply of doctors must be fairly apportioned between them. The Office of War Information made its survey in some sixty communities in twenty states where shortages of doctors have been reported.

OWI representatives traveled through the South, the Midwest, the West, the Eastern Seaboard—in three distinct types of communities: farming regions, where health problems existing for years have been intensified by war; small, quiet, towns that have mushroomed overnight into close packed centers around war industry and military encampments; large cities where ordinary congestion has been aggravated by war activity.

CONCLUSIONS

From first hand operation, from the examination of authentic figures, from protracted inquiries in these communities, the following conclusions emerge:

1. Although there are areas critically in need of doctors because of withdrawals for the armed forces—a need frequently increased by expansion of population for war industry—so far the health of the nation as a whole has not been seriously impaired by the doctor shortage. Doctors these days are not only working overtime; they are—most of them—working practically all the time and in total disregard of their own health.

2. The number of communities critically in need of doctors is not great compared with the total number of communities in the United States. Those in need are, however, among those most vital to our war program.

3. In too many cases physicians were recruited for the armed services without sufficient regard for the welfare of the civilian population. There are, however, enough doctors remaining in private practice to give adequate care to the civilian population, provided they can be properly distributed numerically and according to special abilities.

4. The voluntary relocation of physicians from communities where there is an abundance of doctors to areas in acute need of doctors has proved extremely difficult and has not resulted in a solution to the problem.

5. In some communities local medical groups have resisted attempts to relocate outside doctors in their locality.

6. The situation as a whole is not now out of control, but unless remedial steps are taken soon it will grow progressively worse. More physicians will be recruited for the armed forces and doctors in critical areas—many of them elderly—may succumb to exhaustion from overwork.

7. Luxury medicine, to which some Americans have become accustomed, is out for the duration. We can no longer afford to call doctors for imaginary ailments, and we must make the best and most efficient use of the medical facilities we have.

8. Medical shortages are not due in all cases to the war, although frequently the war has intensified them. For instance, many rural areas have never had a sufficient number of doctors. It is not the purpose of this report to recommend that long-standing problems be solved in time of war except as they relate to our progress toward victory.

PLACES VISITED BY OWI REPRESENTATIVES

One of our American traits is "doing the best we can with what we have." This is exemplified in a number of communities visited by OWI representatives. Faced with the possibility of getting along with too few physicians or with none at all, these communities initiated classes in home nursing; they established health centers presided over by trained nurses; they taught infant care to mothers; they encouraged health building activities; through the local chapters of the Red Cross, nurses were supplied when doctors were not available.

One of the first places visited by OWI representatives was on the outskirts of a great aircraft plant near a large Atlantic seaboard city. Originally this community was a small country village about 12 miles from the center of the city. When the aircraft company went into war production, the whole area became a hive of hurrying humanity. As the village itself could not expand to meet the housing shortage, four trailer sites, with 1,500 trailers housing some 5,000 persons, were established. Many of these trailers are homelike, with tiny gardens and fences around them. There is also a housing project, which is being rapidly opened up. The total population for the area is approximately 25,000 and is increasing daily. The natural result of this mushrooming was a doctor shortage, particularly of general practitioners and obstetricians. Something had to be done to provide medical care for these thousands of war workers and their families; in the trailer camps living conditions were especially precarious. A committee consisting of nearby doctors and the county health officer was organized to recommend ways of relieving the situation. There were six doctors living within the immediate area. Four left but were replaced. The committee arranged for nine others nearby to be on call. For three of these it meant setting up new offices in the district. There are, therefore, fifteen doctors now available, all of whom do obstetric work. If it is possible, women about to have children are sent to their home communities. If this is not feasible they are delivered in the trailer, or, if the case is complicated, they are taken to a hospital in the neighboring city. A specialist in obstetrics has recently opened an office in the area and takes cases on a consulting basis when they are referred to him by the local doctors. A trailer has been fitted up by the local doctors at their own expense to serve as a general office. This has some surgical equipment, and each doctor has office hours one day a week. The telephone numbers of all fifteen doctors—the six in the area and the nine from nearby—are posted in all the outdoor telephone booths of the trailer camp and in the project manager's office.

One of the difficulties in this section is that of persuading the people—many of whom come from sparsely settled rural areas—to seek medical care when they need it. Some of them have a distrust of doctors. A public health nurse has been assigned full time to the trailer camps, and one of her jobs is to try to overcome this prejudice. She also does follow-up work for the doctors, checking to see that directions are being carried out, giving advice on child feeding and care, arranging for x-ray examinations and in general being a mother confessor for the family. Many problems of this community still remain to be solved. Postpartum care is one of them. But at least effort has been made to coordinate medical facilities as effectively as possible.

There are many regions where conditions have not been improved. The OWI found sections where there was only one doctor to 5,000 or 6,000 persons, with people frankly apprehensive over what might happen if any number of them became ill at the same time. They found doctors literally working themselves sick attempting to care for the scores of new patients brought to them by a swollen war industry area. They found places—such as a huge bomber plant on the outskirts of a large Middle Eastern city—where the thousands of persons living in trailers have no sewerage system, where sanitary facilities are inadequate and where there is a possibility of drinking water contamination. They found areas where reports by authorities as to the adequacy of medical care and the number of doctors available were completely misleading. One community near the Canadian border—present population 24,000, an important shipping center and adjacent to an Army encampment and several airfields—was reported as having eighteen doctors. Actually but six of these are effective, the others being too ill or too old to continue full time duty. The only surgeon in the community was recently commissioned for service in the Navy. All the

obstetric work is being done by one young doctor crippled by arthritis and heart trouble, who lately had cataracts removed from both eyes. Despite these ailments he is carrying on to the extent that he is actually endangering his life.

In another county on the West Coast, near a navy yard, there has been an increase in population from 44,400 in 1940 to 110,000, and during 1943 it is expected that 25,000 more persons will move into this area. The present ratio of doctors is one to 4,000, not including the Navy personnel, who are cared for by Navy physicians. The hospital situation is critical, revolving around antiquated equipment, one hospital having 108 beds and another, a private hospital, 18. The larger hospital is selecting some cases for treatment and turning away others equally in need of care. Hospitals in neighboring cities are high priced, crowded and reached by a long ferry or automobile ride. There are eight hundred trailers in this area. People living in them are having a difficult time keeping warm and protecting themselves against insanitary conditions. There are also housing projects where 6,000 people live; eventually 7,500 more people will live there in new projects. But regulations limit occupancy to war workers, and there are many workers essential to the community—such as bus drivers, grocers and policemen—who are not eligible for the project houses. Many among the several thousand women employees of the nearby navy yard, unaccustomed to performing manual work, have developed ailments which, although in most cases minor, demand treatment. Yet Navy doctors and the Navy hospitals are authorized to extend routine medical care only to male industrial casualties; women are treated only in emergencies. In all other cases they are expected to find their own doctor and go to the local hospital.

In one large Middle Western city it was found that a serious situation was relieved by the success of the county medical society in persuading outside doctors to come there. The site of important war plants with consequent increase in population, the city in some sections has a ratio of only one doctor to 5,000 persons, although the total ratio is one to 1,170. The county medical society journal carried appeals to physicians to settle in this city, with the result that four already have done so and two more are arriving in the near future. Two doctors who were recruited by the Army have been allowed to return to private life, and their resumption of practice will further help the situation.

RELOCATION

Relocation of doctors to areas in need is never a simple procedure. Rural areas where there were too few doctors before the war were usually in low income sections which had never been able to support a doctor properly. Physicians are not willing, for the most part, to leave lucrative practices to move to such areas; the difficulty of finding modern housing for their families frequently adds to their hesitancy in relocating. Doctors who already have gone to war sometimes—and quite understandably—show a definite antipathy to permitting outside doctors to come into their home communities and take over their practice. This is illustrated by a petition from members of a county medical society in a Southern state who are now with the armed forces. The petition reads in part:

> We, . . . having abandoned our homes and practices for service in the armed forces of our country, believe that we have the right to demand protection of our practices, and do therefore petition . . . that any doctor under 45 years of age moving into..... County immediately be put on the available list and quickly inducted into the service. . . .

This system, whereby a physician is "put on the available list and quickly inducted into the service," after being declared not essential to his community by the Procurement and Assignment Service, is one method for obtaining doctors for the Army and Navy. It is a system which, in combination with other factors, has resulted in too many doctors being taken from some sections and not enough from others. The U. S. Public Health Service can, under certain conditions, send physicians as commissioned officers into areas of need. Usually this action follows a disaster, such as fire, flood or epidemic. In the present emergency the Public Health Service has sent three physicians and one dentist into critical areas. There are, however, no more funds available to the Public Health Service for this purpose. One of these physicians may have to be withdrawn because of budgetary restrictions. An added difficulty, found in a number of instances by the OWI, is the disinclination of medical groups to allow a physician paid by the Public Health Service to practice medicine in a particular community.

The system in use at present to apportion doctors between the armed forces and the civilian population is inadequate. This system was set up in October of 1941 with the creation of the Procurement and Assignment Service, a committee of four doctors and one dentist, in the Office of Defense Health and Welfare Services. This committee, which was transferred to the War Manpower Commission the following April, was charged with supplying doctors for the armed services while maintaining an adequate supply for the civilian population.

The Procurement and Assignment Service works through state and local committees of leading doctors, whose responsibility it is to declare doctors of military age either "essential" to their communities or "available" to the armed services. Procurement and Assignment has no authority either to assign a doctor to the armed forces or to keep him in practice in his home community. At present, however, neither the Army nor the Navy will grant a commission to a physician until that physician has been declared not essential to his community by Procurement and Assignment.

On April 21, 1942 the War Manpower Commission announced that the Procurement and Assignment Service had started its machinery to secure sixteen thousand physicians for the armed forces before the end of 1942 without weakening the medical structure for civil and industrial population. Of these, five thousand were to be obtained within the next sixty days. In June the goal for 1942 was increased to thirty-five thousand physicians. As the armed forces were enlarged, Procurement and Assignment could not obtain physicians rapidly enough by this voluntary method. The Army in April dispatched recruiting teams through the United States to stimulate recruiting of doctors. These teams recruited at the rate of about one hundred physicians a week. In certain cases pressure was applied to doctors who were reluctant to enter the service. If a doctor was declared not essential to his community by the Procurement and Assignment Service, that doctor, if within the age limit, was expected to apply for a commission. If he did not apply, his status was reported to the draft board and reclassification recommended. A Chicago physician last January was ordered by his draft board to report for induction into the Army as a private in one of the few such actions in the nation. The doctor had been declared available for military service by the Procurement and Assignment Service, and when he failed to file an application for a commission his draft board was advised by the state Selective Service medical director that he could be taken. Three deferments were granted the doctor after he reported for induction and subsequently he filed for a commission.

Usually, doctors needed no pressure to enlist in the service of their country. They went because they felt it was their duty. These voluntary enlistments, combined with urging by Army recruit boards, resulted in severe depletion of physicians in some areas. Especially was this true of the South and of small rural communities, the very places which needed their doctors most.

THE QUOTAS OF VARIOUS STATES

A quota was set in each state for the recruiting of doctors, and the states were not supposed to go beyond these quotas. In many cases they did. Procurement and Assignment committees in two Southern states were not even aware of their quotas until they were oversubscribed. Another factor in uneven withdrawals was the failure to establish the quotas until after the Army recruiting teams began their work of urging doctors to accept commissions. As of Dec. 1, 1942 thirty-eight states and the District of Columbia had gone over their quotas. Alabama went 109 per cent over, Arizona 64 per cent over, Arkansas 27 per cent over, Colorado 28 per cent over, Delaware 59 per cent over, the District of Columbia 4 per cent over, Florida 23 per cent over, Georgia 54 per cent over, Idaho 73 per cent over, Illinois 2 per cent over, Indiana 35 per cent over, Iowa 27 per cent over, Kansas 23 per cent over, Kentucky 70 per cent over, Louisiana 118 per cent over, Maine 32 per cent over, Maryland 14 per cent over, Michigan 50 per cent over, Minnesota 5 per cent over, Mississippi 63 per cent over, Missouri

15 per cent over, Montana 22 per cent over, New Jersey 18 per cent over, New Mexico 129 per cent over, North Carolina 65 per cent over, North Dakota 14 per cent over, Ohio 24 per cent over, Oklahoma 35 per cent over, Oregon 24 per cent over, Pennsylvania 5 per cent over, South Carolina 76 per cent over, South Dakota 41 per cent over, Tennessee 73 per cent over, Texas 57 per cent over, Utah 21 per cent over, Virginia 42 per cent over, Washington 40 per cent over, West Virginia 61 per cent over and Wyoming 71 per cent over. Nine states as of Dec. 1, 1942 were under their quotas: California, Connecticut, Massachusetts, Nebraska, Nevada, New Hampshire, New York, Vermont and Wisconsin. Rhode Island had just 100 per cent of its quota. The Procurement and Assignment Service has announced that recruiting of physicians for the armed forces during 1943 will take place only in those states in which no over-all shortage of physicians exists.

As far as relocations are concerned, the Procurement and Assignment Service is now doing what it can under the handicaps imposed. On December 15 last a statement by Procurement and Assignment contained this: "Procurement and Assignment Service cannot, in all probability, secure on a voluntary basis all the physicians required for private practice, for industry and for staffs in institutions and agencies. Oftentimes where the need is most acute the conditions of practice are not attractive financially or otherwise. Physicians will neither seek nor be sought by some communities where, nonetheless, medical services are needed. Under such circumstances it may be necessary to invoke compulsion." Thus far, no means of invoking that compulsion has been devised.

There are five categories in the manpower pool from which doctors can be drawn to assist the relocation process. Those possibly available are (1) physicians in communities which can "make do" with fewer doctors, (2) interns and residents with physical disabilities which prevent military service, (3) physicians who have retired from practice but are willing to resume, (4) women doctors and (5) refugee doctors.

The Public Health Service has estimated that there are some eight thousand women physicians in the country, none of whom are at present eligible for military service. Some of the women doctors, of course, are not in practice. There are approximately six thousand refugee doctors in the country; several thousand of these are licensed to practice in the states where they reside. Because they are not citizens of the United States, they are not permitted now to accept commissions in the Army or the Navy.

Procurement and Assignment last December and January held meetings throughout the country in an effort to get doctors to relocate voluntarily to areas of need. It reported three hundred and forty physicians relocated through its efforts during 1942 and two hundred and forty-seven relocated by other means.

England in the early days of the war depended, as we do now, on voluntary relocation. England now has authority to send physicians where needed on recommendation of the Central Medical War Committee, although so far doctors generally have relocated without compulsion. It should be pointed out that England—unlike the United States—has a sweeping manpower law which gives the government power to require all persons to "place themselves, their services and their property at the disposal of His Majesty." Thus the minister of labor may direct any person of any age to perform any service which that person is capable of performing.

Because of our federal system and the individual laws of the separate states, the problems of relocation in this country are somewhat more involved than in Great Britain. Normally a physician from one state cannot practice in another without passing that state's medical tests. There are exceptions, such as reciprocal agreements, practice by Public Health doctors under federal commission, and enactment by state legislatures of a law permitting out of state physicians licenses which would expire with the end of the emergency. Such a law has been recommended by Procurement and Assignment to state legislatures for enactment when necessary. Very few legislatures have taken action.

The personal element is also important in attempting relocations. Not only do people become accustomed to a particular doctor—"and he's the only doctor who really understands my condition"—but doctors also become attached to communities. It is hard for a physician long established in one place to uproot himself and his family and go to another in greater need of his services. The only answer to this is, of course, that in war many things are hard for many people but they have to be done just the same. One fact which should be realized is that "luxury" medicine is out for the duration. Doctors will have to restrict their attentions to those actually in need of them, and patients must no longer insist on one particular "favorite" physician.

The problem of medical care in rural regions is quite different from the problem in cities or in large industrial areas. This is recognized by Procurement and Assignment, which has set smaller quotas of physicians for the armed forces in states whose population is distributed over many miles. Unfortunately, in many of these very states recruitment of doctors has been beyond the quotas established.

A COMMUNITY IN A SOUTHERN STATE

A typical case history of a rural community expanding under war industry with consequent intensification of medical shortages was found in a Southern state. In considering this example, as well as in considering other examples, it should be remembered that areas investigated were those where doctor scarcity had been specifically reported. The people of this community before the war were tenant farmers living in poverty. The several textile mills were, for the most part, closed during the depression years. Tuberculosis is prevalent. The manager of one of the textile mills said "The people around here have no vitality." Before the war this community had a population of approximately 40,000 and was medically undersupplied. Now the textile mills are going full blast and a large chemical warfare and an ordnance plant, supervised by the government, have located on the outskirts. There has been a huge influx of workers who are living in crowded and sometimes insanitary conditions. The population has increased to roughly 55,000. With this increase of more than 35 per cent there has been a decrease of one third in the number of effective doctors. Four went into the Army and one died recently. There is now approximately one doctor to each 3,200 persons. Of those available at present, three are 65 years old or older and one is ill and capable of only part time practice. The health department in this community has undertaken a drive to establish sanitary conditions in the most crowded sections, many of the houses have never had toilets or running water, and workers are being jammed into shacks and abandoned stores for lack of other accommodations. As more workers move in and fatigue reduces resistance to disease, the situation may become more serious. A responsible doctor in this community told the OWI that although the doctors were very much overworked he would be reluctant to bring in "outsiders." Asked about the possibility of using women doctors, he said they "might be willing to try one." When the question of refugee doctors was brought up, the doctor replied "Absolutely not. We will not have those men coming in here, taking the places of our men in the Army."

A number of doctors questioned were against allowing refugee physicians to practice in their communities, despite the obvious need for additional medical care.

One area visited in the Middle South has a population of 12,000 and at present is entirely without a doctor. The nearest hospital—a small private one—is 20 miles away. Twenty years ago the country thereabouts was swamp and thicket. A big drainage project opened up the county and brought in land speculators. The population has increased 700 per cent in the past twenty years. Most of the inhabitants are cotton farmers. The one doctor who had been serving this entire area was recently declared nonessential to his community by Procurement and Assignment. He therefore applied for a commission as a doctor in the Army and was accepted. Before he left, however, he brought another doctor—a friend—to this community. The man was 28 years old and within a few months he also was taken by the Army.

The people of this community have tried all possible ways to get their original doctor released by the Army, but without success. They have appealed to Procurement and Assignment for a doctor willing to relocate there but none has been found. The area would not attract the average doctor. There is no

hospital, no nurse. The rough roads make travel most difficult. Frequently the regular physician, before he was called to the Army, went on a night call riding on a tractor. For childbirth cases this doctor carried a folding delivery table. His wife, a trained nurse, went with him. For a clinic he had a small four room brick building next to the drugstore on the main street, of which he was as proud as another doctor might be of the finest metropolitan hospital. Now the clinic is deserted. In the small waiting room dust lies thick on the oak desk and the chairs. The examining room with its operating table, baby scales and enamel cupboard is covered with dust. The druggist next door is doing his best to carry on. Now he practices emergency medicine, for there is no one else to do it. "I may go to jail for this," he says, "but somebody has to take care of the people." The mayor of the town is standing by him—not only standing by, but helping when he has to. The night before the OWI representative visited the town a man came into the drugstore with a deep head wound. The druggist poured on iodine and pasted the gash together with adhesive tape. Another night a woman was brought in severely lacerated and bleeding profusely. The druggist got his friend the mayor, and together they did what they could, keeping life in the woman until she could be taken to the hospital 20 miles away.

Rural regions which are not defense areas are finding it very difficult to obtain doctors. This particular section is not classed as a defense area, as short staple cotton is not considered a war commodity. The cities in this state are fairly well supplied with doctors and fourteen doctors have been relocated, four of them in communities where there are factories making arms and ammunition. The state Procurement and Assignment chairman has received a number of applications from doctors willing to go into war plants as industrial physicians, where they would work eight hours a day for a fixed salary. But there are few applications for relocation to rural districts, where a doctor may have to ride to his patient on a tractor.

A similar problem was found in another Southern state. In a county with a population of some 15,000, the only industry is cotton textile manufacturing. There is no war industry, and no increase in population; therefore, under the present system, this section is unlikely to get emergency aid. Yet the situation here is desperate. In 1941 this county had six doctors. Three of these were taken by the Army. One of the doctors still there is 74 and suffers from a disability which limits his practice to ordering prescriptions over the telephone from druggists. Of the two doctors remaining, one lives on the far eastern side of the county. On the other falls practically all the medical work of the area. He averages about three hours' sleep a night. He tells prospective mothers quite frankly that he will do the best he can for them but he cannot promise to be on hand in a crisis. In 1 case when arrangements had been made long in advance the doctor arrived three days after the birth of the child.

The women of the county take courses in home nursing and nutrition. They are doing the best they can. Through the state Procurement and Assignment the manager of the cotton mill secured the names of eleven doctors who had signified their willingness to be relocated. The manager wrote to all of them, pointing out that the doctor would have charge of the mill's medical service as well as private practice and could make a minimum of $8,000 his first year there. Only one of the eleven answered—a young man who had just finished his internship and had been rejected by the Army. He paid the county a visit. For a time hope rose high among the residents. Then one day the mill manager received a letter. Because of the lack of hospital facilities in the county the young man had decided to locate elsewhere. They are still trying to get a doctor.

A NEED FOR GENERAL PRACTITIONERS

The age of specialization in medicine also has had an effect on doctors who might be available for relocation. OWI representatives discovered time and again a need for general practitioners, even in cities otherwise well supplied with doctors. In some cities it was found that the actual ratio of physicians to population was well within the one to 1,500 ratio established as a guiding figure for the nation as a whole, and yet there was in reality a medical shortage because of a lack of general practitioners, many of whom were taken by the armed forces.

Brig. Gen. Larry B. McAfee, assistant to the Surgeon General of the Army, has stated that 6.5 doctors for each thousand soldiers is the lowest ratio the Army feels is consistent with efficiency. The ratio as of last December was slightly less than 8 per thousand.

As of Sept. 30, 1942 there were considered to be 135,932 effective physicians in the United States. The total number of physicians was 179,039, but some of these are of advanced age, are suffering from physical disabilities or for other reasons are not practicing. There were on active duty with the Army 31,400, with the Navy 6,104 and in the U. S. Public Health Service 1,069, a total of 38,573. Since Sept. 30, 1942, the date of this estimate, additional doctors have been enlisted. Procurement and Assignment has estimated that if the ratio of one physician to each 1,500 persons in the country is preserved —and this ratio is simply a measuring stick susceptible to variations—the maximum number of physicians who can be withdrawn from civil practice during 1943 is 11,455.

In a number of communities investigated, groups of nurse's aides—patriotic townswomen who are trained to perform simple nursing duties in hospitals and clinics and thus relieve registered nurses for more important work—were of distinct help in relieving a nurse shortage. These women, many of them housewives, give patients baths, take temperatures, serve meals and carry out other routine duties which otherwise would occupy the time of a regular nurse. Efforts are being made in other communities to recruit more women for this work. As additional nurses are called for service with the armed forces, the work of these nurse's aides is becoming increasingly important.

Besides this method of alleviating the situation, the OWI found many instances of "making do with what we have." These include posting the names of available doctors in prominent places; agreements among certain doctors to be on call during alternate periods of the day; teaming of doctors, particularly in rural areas, so that a doctor nearest a patient will take a call; creation by doctors of an alternating system for night calls, so that at least one doctor will be on duty at all times; establishment of group clinics. Public health nurses are helping with baby deliveries doing follow-up work for doctors and educating the public in child care and other health programs. Newspapers in many localities periodically campaign for public cooperation in conserving doctors' time.

In one community near a huge Army encampment this "make do" plan has been unusually successful. The situation here was similar to many others found to exist around large military training centers. Thousands of women and children, the families of soldiers and civilian workers at the camp, have invaded the area, creating serious problems of housing, sanitation, water supply and eating facilities in addition to the problem of medical care. In this particular area, in which the fort is permanent but has been vastly expanded, the population of the county has increased from 26,604 in 1940 to about 40,000. There are thirteen doctors practicing in the county, nine of them in the most thickly settled area around the post. Although the ratio is roughly one doctor to 3,000 persons, this is deceptive; eight of the thirteen doctors are 60 years old or over and one of them is 80. Four of the eight practice only half time or less. Families of service men and of civilian workers have not been eligible for medical care at the post since October 1942.

A housing development adjacent to the post has for some time been seeking a doctor but in vain. Recently this community decided to take things into its own hands. It advertised in the Army post newspaper and on the post bulletin board for registered nurses. Three responded—wives of army officers. The community hired two of these and set up an emergency aid station with the aid of Army Emergency Relief funds. The nurses have office hours twice a day, make house calls and hold a baby clinic once a week. Last December they handled 892 calls—520 at the clinic and 366 in homes. Forty-five of the calls were at night. Twenty cases were referred to a doctor obtained from another community. In the beginning supplies and equipment were lent by the post medical authorities, and transportation for the nurses was supplied by the

Red Cross. Now the community is providing both out of its own funds. Plans are under way to enlarge the service by opening another emergency station and hiring the third nurse. The community still hopes that a doctor will relocate there.

THE GROUP PLAN

Prepaid insurance for doctors' care is being utilized by thousands of war workers, particularly on the West Coast, where there are areas as critically in need of doctors as anywhere in the United States. Before the war began, medical societies of two West Coast states were supporting group plans for industrial workers, group plans which have proved increasingly beneficial as population figures grew. Doctors throughout these states who cooperate in the plans are assigned to care for groups of individuals and are paid by funds from the association.

The group plan in one of these states is proving especially capable of adapting itself to the rapidly changing needs of the population. Before the war, medical insurance was provided for industrial workers and farmers. Now this has been extended to take care of residents of emergency housing projects. It was found that many housing units had been located in regions where the available doctors were already taxed to the limit of their endurance, where the distance from the project to doctors' offices was too great and where most residents were migrants unable to work out their medical care problems in new surroundings without help. For such "mushroom" communities the statewide physicians' service and the Federal Public Housing Authority have cooperated in a plan which brings onto the grounds of the housing project itself a resident doctor, who is paid on straight salary basis, and nursing staff. For special care beyond the resident doctor's attention, patients are referred to a panel of local physicians who cooperate in the state service program. The plan embraces a wide variety of medical treatment, chronic illness, hospital treatment, antepartum care, childbirth and much more. The FPHA collects dues along with the rents. Thus the medical profession itself has adapted a group care plan to an important war emergency. So far, it operates in four large and congested areas of this state, where not quite 90 per cent enrolment of housing project residents has been reached. War workers elsewhere in the state may soon be given doctors' help under this plan.

Employers holding war contracts have shown widely divergent attitudes toward safeguarding the health of their workers, ranging from complete indifference to highly conscientious and efficient action. Here again the West Coast offers examples of outstanding achievement. One shipbuilder surveyed the medical facilities of the communities in which his yards were to be built just as he surveyed all other facilities which would affect either his men or his materials and ultimately his production. In some places the local doctors and hospitals seemed numerous enough to care for the incoming workers, but in two districts where a shortage of both doctors and hospitals appeared unavoidable the employer decided to build his own hospital and hire his own staffs of doctors and nurses. Over 100,000 workers in the shipyards which these two hospitals serve pay a fee each week for medical care. This is deducted from wages. Currently nearly 150,000 treatments are given each month by seventy-two doctors and nearly two hundred and fifty nurses. In addition to the two main hospitals and one field hospital, first aid stations are operated throughout the yards which provide quick attention to injuries and also offer preventive medicine, which considerably reduces the illness rate and the time required away from work for treatment.

The general conclusion drawn from this investigation is that while there is not at present a serious breakdown in the health of the nation due to the doctor shortage there is a probability of slow deterioration of health in communities suffering from medical shortages. Long hours of work in war plants are a contributing factor in health breakdown. The problem of absenteeism in war factories due to illness is a serious impediment to the success of the war.

It is also evident that we can no longer afford to look tolerantly on the scarcity of medical care in rural areas. Farmers have become as important as the man on the fighting front or the man in a shell factory.

Antepartum and postpartum care for mothers has assumed added importance. And, as is usual in wartime, our birth rate is soaring. These new citizens must be properly cared for, as must their mothers, thousands of whom are working side by side with their menfolk in war plants.

The medical situation in this country as a whole is not now serious. It can, however, interfere with our war production unless we initiate some method of appraising the problem in its entirety and deciding on the best plan for meeting it.

The war has brought many new problems to America and has intensified old ones. Comparisons with what happened to this country during the last war are frequently unavailing, for this war is not like the last war. It is infinitely more difficult, it involves infinitely more people. It cannot be run successfully on a makeshift basis. Whenever possible, problems must be met—and in many cases are being met—before they develop into serious situations. Recognition that a medical problem exists before it reaches the danger stage is all important.

It is recognized that relocation of doctors is not the whole answer to the problem of medical care for the civilian population in wartime. Nurses, hospitals, clinics, nutrition, sanitation, preventive medicine all play vital parts. To these subjects the Office of War Information may return in a later report.

MISCELLANEOUS

PUBLIC HEALTH UNDER HITLER

According to NDZ of January 20, in the *Gesundheitsfuehrung*, the president of the Reich Board for the Fight Against Rheumatic Ailments, Prof. Dr. Geronne, stresses the great social importance of this work. About 12 per cent of all cases of illness in large enterprises are due to rheumatic diseases. The significance of this from the social point of view is not so apparent in the death rate as in the large number of resulting cases of heart disease. The most important problem is early diagnosis and early treatment of rheumatic ailments. Health insurance societies must be obliged to keep a special register of these cases of illness. It is necessary too to organize large sections in hospitals to deal with cases of rheumatic disease. For the time being it will probably suffice to open three or four of these special sections in each gau, with the object of procuring the best possible early treatment and, at the same time, continuing the training of doctors. The campaign against rheumatic ailments will start with the setting up of these special sections in hospitals in all gaue. In addition, it will be necessary later on organize observation centers in suitable hospitals. These will collaborate with the special sections in their practical work. Finally, preventive measures must be extended by popular enlightenment, strengthening resistance, promotion of physical fitness, care of the teeth and hygienic working and living conditions.

NDZ of January 18 states that in the fight against tuberculosis series of x-ray examinations made with the schirmbildgerat have proved the best means of discovering the persons suffering from this disease. To insure that the scheme is carried out systematically, the reich health leader has issued an order stating that the examination of the population by means of x-ray series photos will be undertaken by the x-ray sturmbann. These examinations include all examinations of the inhabitants of densely populated centers, especially of entire gaue towns and kreise. They do not comprise examinations of certain groups of the population which are made by the health offices, or of party formations, factory workers and civil servants. The reich health leader has created within his office a service unit for x-ray series examinations of the people, consisting of party members Drs. Blome, Walter and Holfelder. This service unit will be responsible for the execution of the scheme.

According to *Zora* of January 5, the government has fixed prices for medicines and will pay the difference between the fixed price and the cost price from the equalization fund.

ORGANIZATION SECTION

THE HOUSE OF DELEGATES SESSION

AMERICAN MEDICAL ASSOCIATION, CHICAGO

BEGINNING JUNE 7, 1943

OFFICIAL CALL

TO THE OFFICERS, FELLOWS AND MEMBERS OF THE AMERICAN MEDICAL ASSOCIATION

The regular annual session of the House of Delegates of the American Medical Association will be held in Chicago, beginning Monday, June 7, 1943.

In the House the representation of the various constituent associations for 1941, 1942 and 1943 is as follows:

Alabama	2	New Hampshire	1
Arizona	1	New Jersey	5
Arkansas	2	New Mexico	1
California	8	New York	19
Colorado	2	North Carolina	3
Connecticut	2	North Dakota	1
Delaware	1	Ohio	7
District of Columbia	1	Oklahoma	2
Florida	2	Oregon	1
Georgia	3	Pennsylvania	11
Idaho	1	Rhode Island	1
Illinois	9	South Carolina	2
Indiana	4	South Dakota	1
Iowa	3	Tennessee	2
Kansas	2	Texas	5
Kentucky	3	Utah	1
Louisiana	2	Vermont	1
Maine	1	Virginia	2
Maryland	2	Washington	2
Massachusetts	6	West Virginia	2
Michigan	5	Wisconsin	3
Minnesota	4	Wyoming	1
Mississippi	2	Alaska	1
Missouri	4	Hawaii	1
Montana	1	Isthmian Canal Zone	1
Nebraska	2	Philippine Islands	2
Nevada	1	Puerto Rico	1

The sixteen scientific sections of the American Medical Association, the Medical Corps of the Army, the Medical Corps of the Navy and the Public Health Service are entitled to one delegate each.

There will be no Scientific Assembly of the Association in 1943, but the President-Elect, Dr. James E. Paullin, will be installed as President in the Ball Room of the Palmer House, Chicago, at 8 p. m., Tuesday, June 8, 1943.

FRED W. RANKIN, President.
H. H. SHOULDERS, Speaker, House of Delegates.
OLIN WEST, Secretary.

MEMBERS OF THE HOUSE OF DELEGATES

A Preliminary Roster of the Legislative Body of the American Medical Association

The list of members of the House of Delegates for the session is incomplete, as a number of the state associations are yet to hold their meetings at which delegates will be elected. The following is a list of the holdover members of the House of Delegates and of the newly elected members who have been reported to the Secretary in time to be included:

STATE DELEGATES

ALABAMA
Lloyd Noland, Fairfield.
A. A. Walker, Birmingham.

ARIZONA
Harold W. Kohl, Tucson.

ARKANSAS
Edward E. Barlow, Dermott.

CALIFORNIA
Edward N. Ewer, Oakland.
Robert A. Peers, Colfax.
William R. Molony Sr., Los Angeles.

COLORADO
John Andrew, Longmont.
Walter W. King, Denver.

CONNECTICUT
Thomas P. Murdock, Meriden.
James R. Miller, Hartford.

DELAWARE
Laurence L. Fitchett, Milford.

DISTRICT OF COLUMBIA
Henry C. Macatee, Washington.

FLORIDA
Meredith Mallory, Orlando.
Edward Jelks, Jacksonville.

GEORGIA
Olin H. Weaver, Macon.
William A. Mulherin, Augusta.
Allen H. Bunce, Atlanta.

IDAHO
Edward N. Roberts, Pocatello.

ILLINOIS
Edwin S. Hamilton, Kankakee.
Charles H. Phifer, Chicago.
John J. Pflock, Chicago.
G. Henry Mundt, Chicago.
Rollo K. Packard, Chicago.

INDIANA
Don F. Cameron, Fort Wayne.
F. S. Crockett, La Fayette.
H. G. Hamer, Indianapolis.
George R. Dillinger, French Lick.

IOWA
Thomas F. Thornton, Waterloo.
Arthur D. Woods, State Center.

KANSAS
Forrest L. Loveland, Topeka.
J. F. Hassig, Kansas City.

KENTUCKY
Virgil E. Simpson, Louisville.

LOUISIANA
James Q. Graves, Monroe.
Leon J. Menville, New Orleans.

MAINE
Thomas A. Foster, Portland.

MARYLAND
Alfred T. Gundry, Baltimore.
Thomas S. Cullen, Baltimore.

MASSACHUSETTS
David D. Scannell, Boston.
Dwight O'Hara, Boston.
Charles E. Mongan, Somerville.
Walter G. Phippen, Salem.
Allen G. Rice, Springfield.
Richard H. Miller, Boston.

MICHIGAN
Leo G. Christian, Lansing.
Frank E. Reeder, Flint.
Henry A. Luce, Detroit.
T. K. Gruber, Eloise.
Claude R. Keyport, Grayling.

MINNESOTA
James M. Hayes, Minneapolis.
Francis J. Savage, St. Paul.
W. A. Coventry, Duluth.
A. W. Adson, Rochester.

MISSOURI
Arthur R. McComas, Sturgeon.
Warren L. Allee, Eldon.

MONTANA
J. H. Irwin, Great Falls.

NEBRASKA
Roy W. Fouts, Omaha.
Karl S. J. Hoblen, Lincoln.

NEW HAMPSHIRE
Deering G. Smith, Nashua.

NEW JERSEY
Andrew F. McBride, Paterson.
Lucius F. Donohoe, Bayonne.
Thomas K. Lewis, Camden.
Hilton S. Read, Ventnor.
Wells P. Eagleton, Newark.

NEW MEXICO
H. A. Miller, Clovis.

NEW YORK
Louis H. Bauer, Hempstead.
James M. Flynn, Rochester.
George W. Kosmak, New York.
Thomas A. McGoldrick, Brooklyn.
Samuel J. Kopetzky, New York.
John J. Masterson, Brooklyn.
John T. Donovan, Buffalo.
Frederic E. Sondern, New York.
Walter W. Mott, White Plains.

NORTH CAROLINA
William T. Rainey, Fayetteville.
Wilburt C. Davison, Durham.

OHIO
George A. Woodhouse, Pleasant Hill.
Harry V. Paryzek, Cleveland.
Carl R. Steinke, Akron.

OKLAHOMA
Walter A. Howard, Chelsea.

OREGON
John H. Fitzgibbon, Portland.

PENNSYLVANIA
Charles G. Strickland, Erie.
Robert L. Anderson, Pittsburgh.
J. Newton Hunsberger, Norristown.
William L. Estes Jr., Bethlehem.
Joseph Scattergood Jr., West Chester.
Alexander H. Steward, Harrisburg.
Francis F. Borzell, Philadelphia.
James H. Corwin, Washington.

Walter F. Donaldson, Pittsburgh.
Charles H. Henninger, Pittsburgh.
Leonard G. Redding, Scranton.

RHODE ISLAND
Guy W. Wells, Providence.

SOUTH CAROLINA
Joseph H. Cannon, Charleston.

SOUTH DAKOTA
Nelius J. Nessa, Sioux Falls.

TENNESSEE
Elbert G. Wood, Knoxville.

TEXAS
Howard R. Dudgeon, Waco.
Alonzo A. Ross, Lockhart.
Edward H. Cary, Dallas.

UTAH
John Z. Brown, Salt Lake City.

VERMONT
Benjamin F. Cook, Rutland.

VIRGINIA
Walter B. Martin, Norfolk.
J. Morrison Hutcheson, Richmond.

WASHINGTON
John H. O'Shea, Spokane.
R. L. Zech, Seattle.

WEST VIRGINIA
Ivan Fawcett, Wheeling.
Walter E. Vest, Huntington.

WISCONSIN
Joseph F. Smith, Wausau.
Stephen E. Gavin, Fond du Lac.
James C. Sargent, Milwaukee.

WYOMING
George P. Johnston, Cheyenne.

HAWAII
F. J. Pinkerton, Honolulu.

DELEGATES FROM THE SECTIONS AND GOVERNMENT SERVICES

PRACTICE OF MEDICINE
Fred M. Smith, Iowa City.

SURGERY, GENERAL AND ABDOMINAL
Henry W. Cave, New York.

OBSTETRICS AND GYNECOLOGY
Jean Paul Pratt, Detroit.

OPHTHALMOLOGY
Arthur J. Bedell, Albany, N. Y.

LARYNGOLOGY, OTOLOGY AND RHINOLOGY
Burt R. Shurly, Detroit.

PEDIATRICS
William Weston, Columbia, S. C.

EXPERIMENTAL MEDICINE AND THERAPEUTICS
O. P. J. Falk, St. Louis.

PATHOLOGY AND PHYSIOLOGY
L. W. Larson, Bismarck, N. D.

NERVOUS AND MENTAL DISEASES
Henry R. Viets, Boston.

DERMATOLOGY AND SYPHILOLOGY
Clyde L. Cummer, Cleveland.

PREVENTIVE AND INDUSTRIAL MEDICINE AND PUBLIC HEALTH
Stanley H. Osborn, Hartford, Conn.

UROLOGY
Roy B. Henline, New York.

ORTHOPEDIC SURGERY
J. Archer O'Reilly, St. Louis.

GASTRO-ENTEROLOGY AND PROCTOLOGY
Louis A. Buie, Rochester, Minn.

RADIOLOGY
E. H. Skinner, Kansas City, Mo.

ANESTHESIOLOGY
H. S. Ruth, Merion Station, Pa.

UNITED STATES ARMY
Larry B. McAfee, Washington, D. C.

UNITED STATES NAVY
Harold W. Smith, Washington, D. C.

UNITED STATES PUBLIC HEALTH SERVICE
Warren F. Draper, Washington, D. C.

OFFICIAL NOTES

DOCTORS AT WAR

Radio broadcasts of Doctors at War by the American Medical Association in cooperation with the National Broadcasting Company and the Medical Department of the United States Army and the United States Navy are on the air each Saturday at 5 p. m. Eastern War Time (4 p. m. Central War Time, 3 p. m. Mountain War Time, 2 p. m. Pacific War Time). An exception is the Chicago area, where the broadcasts are heard by transcription at 10:30 p. m. (formerly heard at 8 p. m.) Saturdays over Station WMAQ.

The titles and guest speakers for the next four programs are as follows:

April 10. "Battle Stations at Home."
Speaker, Col. George Baehr, Chief Medical Officer, Office of Civilian Defense.

April 17. "Stratosphere Flight."
Speaker, Brig. Gen. David N. W. Grant, Air Surgeon, United States Army.

April 24. "Sharp Eyes."
Speaker, Lieut. Col. Harold C. Lueth, Liaison Officer, Procurement and Assignment Service, Chicago.

May 1. "Jungle Death."
Speaker, Brig. Gen. C. C. Hillman, Chief of the Professional Services, Office of the Surgeon General, United States Army.

BEFORE THE DOCTOR COMES

The American Medical Association program on Radio Station WLS (890 kilocycles) entitled "Before the Doctor Comes" will be on the air every Thursday morning at 9:45 up to and including May 27. Common home health problems are discussed in an interview program in which Dr. W. W. Bauer, Director of the Bureau of Health Education, is interviewed by Mrs. June Merrill. The titles for the next four programs are:

April 8. "What to Do About Cuts and Scratches."
April 15. "What to Do About Bad Bumps."
April 22. "What to Do About Choking."
April 29. "What to Do About Bleeding."

MEDICAL LEGISLATION

MEDICAL BILLS IN CONGRESS

Changes in Status.—S. 400 has been reported to the Senate in an amended form with recommendation that it pass, a bill providing for the organization and functions of the United States Public Health Service. One amendment provides that for the duration of the present war and for six months thereafter graduates of reputable osteopathic colleges shall be eligible for appointment as reserve officers in the Public Health Service. S. 495, a bill to establish a Women's Army Corps for service in the Army of the United States, has been reported, with amendments, to the House of Representatives. One amendment provides that physicians and nurses shall not be enlisted in the corps. S. 675 has been reported to the Senate, a bill to amend the Selective Training and Service Act so as to extend the benefits of the United States Employees' Compensation Act to conscientious objectors. H. R. 1857 has been reported to the House with an amendment providing for the commissioning of female physicians and surgeons in the Medical Corps of the Army and Navy. The amendment strikes from the bill the restriction that such female physicians may be assigned to duty only in hospitals or other stations where female nurses are employed. H. R. 1749 has been approved by the President to amend Veterans' Regulations so as to grant hospitalization, domiciliary care and burial benefits to any person who served in the active military or naval service of the United States on or after Dec. 7, 1941 and before the termination of the present war. H. R. 2218 has been reported to the House, a bill to provide a method for the payment currently of individual income taxes. One section of this bill proposes an additional exemption for persons in military or naval service of so much of his service pay as does not exceed the sum of $3,500 over the personal exemption.

Bills Introduced.—The President has submitted to the Congress a supplemental estimate of appropriations for the Public Health Service in the amount of $2,294,000 for pay of personnel and maintenance of hospitals. S. 897, introduced by Senator Bailey, North Carolina, proposes an amendment to the Insecticide Act providing that any white powder insecticide or fungicide containing arsenic in its elemental form or in any of its combinations, or fluorine in any of its combinations, shall, unless deemed unnecessary by the Secretary of Agriculture for the protection of the public health, be deemed to be adulterated unless it is distinctly colored in accordance with regulations promulgated by the Secretary of Agriculture. S. 910, introduced by Senator Downey, California, proposes to amend the Social Security Act so as to provide that each state shall have the exclusive right to adopt its own interpretation of the phrases "needy individuals who are blind" and "blind individuals who

are needy." The purpose of the bill is to encourage the states to make more adequate provision for blind persons. H. J. Res. 103, introduced by Representative Carson, Ohio, proposes the establishment of a Division for the Physically Handicapped in the United States Employment Service. H. R. 2084, introduced by Representative Hagen, Minnesota, would extend the status of veterans of the World War to persons enrolled or enlisted and serving on United States Shipping Board vessels during the World War in war zones. H. R. 2248, introduced by Representative Hare, South Carolina, provides for disability compensation for certain injuries sustained by civil employees of the United States government. H. R. 2251, introduced by Representative Spence, Kentucky, proposes to create a Division of Water Pollution Control in the United States Public Health Service. H. R. 2276, introduced, by request, by Representative Pace, Georgia, proposes an appropriation of $1,000,000 annually for the duration of the emergency for allotment to the states to promote the development of better diets and an improved nutritional status for the people of the United States. H. R. 2285, introduced by Representative Tolan, California, would establish an Office of War Mobilization and create therein an Office of Scientific and Technical Mobilization to effect the full and immediate mobilization of scientific knowledge, technics and personnel for the prosecution of the war and for making adjustments necessitated by war conditions.

STATE MEDICAL LEGISLATION

California

Bill Introduced.—S. 1077 proposes the creation of a state board of naturopathic examiners and defines naturopathy as the treatment of the sick and afflicted by the use of such substances as light, air, water, clay, heat, rest, diet, herbs, electricity, massage, Swedish movements, suggestive therapeutics, magnetism and physical and mental culture. Naturopaths would be authorized to execute birth and death certificates and to have the same rights as other physicians to practice under any governmental plan or system created for the purpose of providing medical care or treatment. Approved naturopathic colleges would have the right to receive dead bodies for the purpose of instruction and study in like manner and under the same provisions of law as other institutions.

Connecticut

Bill Enacted.—S. 261 has become chapter 45 of the Laws of 1943. It amends the premarital examination law by providing that the required certificate shall be signed by a physician licensed to practice medicine or osteopathy in Connecticut or in any other state or territory of the United States or the District of Columbia.

Indiana

Bill Enacted.—S. J. Res. 7 was adopted, February 26. It resolves that the general assembly go on record as urgently requesting the Congress of the United States to pass legislation to establish a pharmacy corps in the army.

Iowa

Bill Enacted.—S. 82 was approved, March 16. It amends the income tax law by authorizing taxpayers to deduct expenses for the medical care of the taxpayer, his spouse or a dependent and defines the term medical care as amounts paid for the diagnosis, cure, mitigation, treatment or prevention of disease or for the purpose of affecting any structure or function of the body.

Kansas

Bills Introduced.—H. 366 proposes to extend the scope of osteopathic practice by authorizing present and future licentiates to administer and prescribe narcotics and biologicals and to register and practice under the laws of the United States governing the administering and prescribing of narcotics. Biologicals are defined as medicinal preparations made from animal juices, tissues or serums. H. 394 proposes to require each applicant for a marriage license to present a certificate from a duly licensed physician certifying that the applicant and the proposed marital partner are, in the opinion of such physician and based on a standard serologic test for syphilis, not incapacitated to marry.

Bill Passed.—H. 332 passed the house on March 3 and the senate on March 17. It proposes to require every physician to take or cause to be taken a sample of blood of any woman whom he diagnoses as being pregnant, such sample to be taken within fourteen days after the diagnosis is made and only with the consent of the patient.

Bills Enacted.—H. 120 was approved, March 10. It excuses physicians in the military service from renewing their licenses annually and prohibits revocation of such licenses during the period of their military service. H. 121 was approved, March 10. It amends the medical practice act by eliminating the requirement that no two of the required four six month periods which must be spent in the study of medicine and surgery may be given within the same twelve months. The purpose of this law is to enable graduates of accelerated medical courses to obtain licensure in Kansas.

Maine

Bill Passed.—S. 304 passed the house, March 10. To amend the osteopathic practice act, it proposes to authorize approved osteopathic schools to give a course of instruction for a total of thirty-six months within a three to four year period when such school has adopted compressed or accelerated courses as a war emergency measure.

Maryland

Bills Introduced.—H. J. Res. 20 proposes a request to the legislative council to make a study looking toward the enactment of a law to reimburse nonprofit hospitals for expenses incurred in treating indigent patients suffering from injuries from automobile accidents. H. 499 proposes the creation of a state board of naturopathic examiners and defines naturopathy as a branch of the healing art embracing the diagnosis and practice of physiologic, physical, mechanical and material methods and agencies of healing. The bill would further provide that nothing therein should be held or construed to authorize any naturopathic physician licensed thereunder to use drugs or surgery. H. 663 proposes to repeal the existing law requiring all children to produce certificates of vaccination before being admitted to any public school.

Bills Passed.—S. 339 passed the senate, March 16. It proposes to prohibit teachers from receiving into the public schools any child between the ages of 5 and 10 who does not present the certificate of a registered practicing physician of the state of Maryland or of the county health officer that such child has received an inoculation of toxoid, or other approved immunizing agent, to protect against diphtheria, at least one of said inoculations having been given after the age of 5 years. S. 360 passed the senate, March 19. It proposes that no persons shall sell, dispense or give away any drug or medicine for the treatment or cure of venereal disease or any sulfonamide drug except on the written prescription of a physician licensed to practice medicine. H. 524 passed the house, March 12. It proposes to require the state department of health to furnish insulin to all residents who are suffering from diabetes and who are unable because of their financial condition to purchase such insulin, provided that any person who is financially able to pay for the drug may obtain it from the state department of health at actual cost.

Massachusetts

Bills Introduced.—H. 1382, to amend the law relating to aid to dependent children, proposes to authorize payment for medical and hospital care to be made directly to the person furnishing such services in certain instances. H. 1387 proposes to authorize the department of public health to establish and maintain cancer clinics and to provide therein services and treatment for cancer.

Michigan

Bills Introduced.—H. 250, to amend the crippled children's act, proposes, among others things, to limit professional fees for major operations to $75 and to $200 for any one physician for any one patient in any year. H. 266 proposes a completely new act providing for the payment of compensation to employees who sustain disabilities from injuries or diseases during the course of their employment. H. 343 proposes to prohibit any minor from purchasing and any person from selling to a minor any alcoholic beverage except pursuant to a prescription

of a duly licensed physican. H. 359, to amend the premarital examination law, proposes to require applicants for a marriage license to present a certificate of a reputable physician to the effect that such person is free from venereal diseases and is mentally sound. H. 373, to repeal certain sections of the existing law relating to the licensing of pharmacists and to reenact a new law on the same subject, proposes, among other things, that the phrase "practice of pharmacy" shall mean the manufacture, compounding, dispensing, sale or distribution of drugs, medicines or poisons to be used for man or other animal.

Bills Passed.—S. 113 passed the senate on March 9 and the house on March 17. To amend the medical practice act, it proposes to authorize the Michigan state board of registration in medicine to suspend in whole or in part the educational requirements prescribed by the act at any time during the state of war now existing between the United States and various other nations. S. 192 passed the senate on March 9 and the house on March 17. To amend the osteopathic law, it proposes to authorize the Michigan state board of osteopathic registration and examination to modify, by order, the educational requirements prescribed by the present act, during the present emergency. H. 264 passed the house, March 11. It proposes that, where persons entitled to hospital service under a contract for such service are unable to obtain admittance to any hospital because of lack of facilities or accommodations, such contract may provide a method by which such persons may be reimbursed in whole or in part for the expense of nursing and other nonmedical care, restricted to the equivalent of hospital care, required from the illness or injury entitling such person to hospital service. H. 277 passed the house, March 20. It proposes to prohibit druggists and pharmacists from selling barbituric acid and any of its derivatives, chloral hydrate or paraldehyde, except on prescription of a licensed physician, dentist or veterinarian.

Minnesota

Bills Introduced.—S. 703 proposes to amend the law prohibiting any county official or deputy or clerk of such official from being directly or indirectly interested in any contract, work, labor or business to which the county is a party or in which it is or may be interested in the furnishing of any article or the purchase or sale of any property, or of which the construction, price or expense is payable from the county by excepting therefrom county coroners, their deputies or county physicians, for medical services performed by them for indigent persons receiving public relief, or in appearing in insanity or incompetency hearings. S. 764 proposes to prohibit any persons from practicing or holding themselves out as practicing the Sister Kenny technic of treating infantile paralysis without first being authorized so to do and further proposes that any registered nurse who has received at least two years' additional training in an accredited institute or hospital using such technic may, on receiving a degree from said institute or hospital, engage in such practice. S. 825, to amend the law relating to coroners, proposes that any coroner or deputy coroner who is a duly licensed and registered physician and surgeon shall not be disqualified from rendering medical care or hospitalization to a recipient of public relief, from being appointed an examiner in insanity or incompetency hearings or from being compensated therefor. H. 334 proposes to authorize licensed insurance companies to write policies to insure against loss or damage for medical, hospital, surgical or funeral expense. H. 362 proposes to prohibit the operation of a nursing home, convalescent home and rest home, for hire, without being authorized so to do by the commissioner of charities and corrections. H. 578 and S. 581 propose to authorize any subordinate lodge of a fraternal organization to provide medical services for members and their families and to contract with physicians to perform such services. H. 718 and S. 564 propose to transfer from the director of social welfare to the director of public institutions all powers and duties respecting mental hygiene work. H. 935 proposes to amend the law requiring corporations to be licensed before being authorized to operate a hospital, nursing home or the like by including municipal corporations, and all state subdivisions, departments, boards and agencies. H. 979, to amend the law relating to the fees of coroners, proposes that physicians called by the coroner to make an autopsy shall be allowed a fee of $15 per day plus mileage and that a coroner or deputy coroner who is a duly licensed physican and surgeon shall not be disqualified from rendering medical care or hospitalization to a recipient of public relief, from being appointed an examiner in insanity or incompetency hearings, or from being compensated therefor. H. 985 proposes to transfer from the director of public institutions to the director of social welfare all powers and duties with reference to the state sanatorium for consumptives.

Bill Enacted.—H. 273 has become chapter 121 of the Laws of 1943. It provides that physicians in the armed forces shall not be required to renew their annual licenses during the term of such service and shall be exempt from payment of all renewal fees.

Montana

Bills Enacted.—S. 63 has become chapter 102 of the Laws of 1943. It authorizes certain institutions of higher learning in Montana to obtain custody of unclaimed human bodies for use in the teaching and demonstration of anatomic science by professional instructors. S. 97 has become chapter 106 of the Laws of 1943. It relieves physicians in the military service of the United States from paying annual license fees during the period of such service. H. 91 has become chapter 125 of the Laws of 1943. It authorizes the creation of a division of Dental Health under the supervision of the state board of health, the director to be a regularly licensed dentist who shall have had at least one school year of training in an accredited school of public health, and the duties of the new division shall be the development and promotion of those activities which result in the protection and improvement of the dental health of the people of the state. H. 118 has become chapter 132 of the Laws of 1943. It amends the medical practice act by authorizing the board of medical examiners to prescribe and enforce reciprocity requirements current with changes in standards of the practice of medicine and surgery. H. 128 has become chapter 126 of the Laws of 1943. It authorizes state, county and local health officers to detain and examine prostitutes, and females suspected of engaging in promiscuous sexual intercourse, who are infected or thought to be infected with a venereal disease, and to require such persons to report for treatment until cured. Such examinations may be repeated as often as deemed advisable or desirable. H. 134 has become chapter 225, Laws of 1943. It amends the law relating to the state board of health by increasing the membership thereof from five to seven, the two additional members to be the president of the Montana state board of pharmacy and the president of the Montana state board of food distributors. It also decreases from five to three years the term of office of the members of such board. H. 245 has become chapter 165 of the Laws of 1943. It amends the law governing insane asylums by providing, among other things, that it shall be the duty of the hospital medical staff to examine all patients who have curable diseases every six months and to file a written report thereof.

Nebraska

Bill Introduced.—Legislative bill 417 proposes to authorize the board of control to place in the Nebraska Institution for the Feebleminded any spastic person when on written application and after due investigation the board is of the opinion it is for the best interests of such person. The proposal would further require that a separate ward for spastic persons be provided at such institution.

Bill Passed.—Bill 40 passed the house, March 23. It proposes to require each applicant for a marriage license to present a certificate signed by a duly qualified physician licensed to practice medicine and surgery in any state or United States territory certifying that the applicant is not infected with syphilis in a communicable stage.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ARKANSAS

Personal.—Dr. William H. Toland, Nashville, has been appointed health officer for Howard County.——Dr. Henry E. Mobley has been elected a director of the Morrilton Chamber of Commerce.——Dr. William G. Hancock, Rison, has been named health officer of Cleveland County.

State Medical Meeting.—The Arkansas Medical Society will hold its annual session in Little Rock, April 19-20. Dr. Rufus B. Robins, Camden, is president of the association. The program includes the following speakers:

Dr. John Harry Hayes, Little Rock, Analysis of Thyroid Surgery.
Dr. Merlin J. Kilbury, Little Rock, Leukemia and Aleukemic Diseases.
Dr. Allie C. Kolb, Little Rock, Care of the Insane in the State of Arkansas.
Dr. Davis W. Goldstein, Fort Smith, Industrial Dermatoses.
Dr. Robert L. Sanders, Memphis, Tenn., Surgery of the Gallbladder and Common Duct.
Dr. John H. Musser, New Orleans, The Doctor's Heart.
Dr. F. Walter Carruthers, Little Rock, New Concepts in the Diagnosis and Treatment of Poliomyelitis.
Dr. Louie G. Martin, Hot Springs National Park, A Safe and Sane Method of Treatment in Neurosyphilis.

CALIFORNIA

New Secretary of California Board of Examiners.—Dr. Frederick N. Scatena, Sacramento, has been elected secretary-treasurer of the California Board of Medical Examiners. He succeeds Dr. Charles B. Pinkham, Sacramento, who retired on February 1 after thirty years' continuous service to the state (THE JOURNAL, January 23, p. 270). Dr. Scatena, who has been a member of the board since 1941, graduated at the University of California Medical School, San Francisco, in 1914. Dr. John R. Walker, Fresno, was recently appointed to the board by the governor to succeed Dr. William A. Swim, Los Angeles, whose term expired.

Arrested for Impersonating a Physician.—Reginald T. King was recently arrested for impersonation of an army officer by agents of the federal bureau of investigation, the Los Angeles *Daily News* reported. He was said to be wearing a caduceus on his army uniform at the time of his arrest. The report stated that King had "dolled himself up in an army uniform, posed as an officer of the medical corps, went lecturing at a high school, assumed the privileges of a doctor in a hospital, attended medical conferences and was very generally accepted." At one time he was a laboratory and x-ray technician in the office of a physician in Vallejo and was listed in the telephone directory as "Dr. R. B. King, 327 Georgia Street." He is reported to have been arrested for practicing medicine without a license and to have served a sentence of nine months in the Los Angeles County Jail. Investigations by the FBI revealed that "he was a doctor at the Naval Pacific Air Base Hospital in Hawaii from June to October 1941," when he was asked to resign. On Dec. 12, 1941 he was arrested by military police and later sentenced by a military tribunal to prison. Court evidence showed that he was not a doctor of medicine but a registered nurse. It is alleged that King used many aliases, including Theodore King, Theodore Bullock and Reginald Belford King.

FLORIDA

State Medical Meeting.—The seventieth annual meeting of the Florida Medical Association will be held at the George Washington Hotel, Jacksonville, April 15-16, under the presidency of Dr. Gilbert S. Osincup, Orlando. Dr. Charles W. Roberts, Atlanta, will address the first general session on "Medical Stewardship in War and Peace." Dr. George Baehr, chief medical officer, U. S. Office of Civilian Defense, Washington, D. C., will speak at the second general session on "British and American Experiences in Civil Defense." Col. Sanford W. French, M. C., U. S. Army, will address the third general session on "The Doctor in the War Effort." Reference committees and the house of delegates will hold sessions on Thursday. The association dinner will be held Thursday evening, and the election and installation of new officers will be held following the third general session on Friday.

GEORGIA

Conservation of Manpower.—A series of industrial health institutes for the conservation of manpower was held in Augusta on March 11, Savannah on March 12, Atlanta on March 15 and Columbus on March 16. The program was sponsored by the Medical Association of Georgia, the state department of public health and the Associated Industries of Georgia and was designed for the physician, industrial management and industrial labor. The local medical society and health department and chamber of commerce cooperated in each institute. Among the speakers who participated in the programs were:

Dr. Thomas F. Abercrombie, Atlanta, Community Health Problems Affecting Industry.
J. J. Bloomfield, sanitary engineer, U. S. Public Health Service, Bethesda, Md., Wartime Health Problems Within Industry.
Dr. Lester M. Petrie, Atlanta, Health Services Available to Industry in Georgia.
A. J. Schroder II, personnel manager, Brunswick Pulp & Paper Company, Brunswick, Management's View of the Physician's Function in Industry.
W. Cicero Kendrick, editor of the *Journal of Labor*, Atlanta, Labor's View of Industrial Health.
Dr. Lloyd Noland, Fairfield, Ala., Recent Developments in the Handling of Industrial Injuries.
F. Ruth Kahl, public health nursing consultant, industrial hygiene section, National Institute of Health, Bethesda, Nursing Aspects of Health Program for Industry.
J. G. Williams, D.D.S., director of the division of dental health education, state department of public health, Atlanta, Dental Aspects of Health Program for Industry.
Dr. Carl M. Peterson, Chicago, secretary of the Council on Industrial Health, American Medical Association, Medical Aspects of Health Program for Industry.
Dr. Raymond Hussey, Baltimore, Occupational Diseases and Their Control.

ILLINOIS

Dr. Pettit Chairman of Cancer Board.—Dr. Roswell T. Pettit, Ottawa, was recently elected chairman of the advisory board to the division of cancer control in the state department of public health to succeed Dr. David J. Davis, dean of the University of Illinois College of Medicine.

Chicago

The Capps Prize.—The Institute of Medicine of Chicago announces that competition is now open for the annual Joseph A. Capps Prize of $400. Graduates of Chicago medical schools who completed full internship or one year of laboratory work in 1941 or thereafter are eligible. The prize is for investigation in medicine or in the specialties of medicine and may also be in the fundamental sciences, provided the work has a definite bearing on some medical problem. Manuscripts must be submitted to the Secretary of the Institute of Medicine of Chicago, 86 East Randolph Street, not later than December 31.

KENTUCKY

Occupational Diseases Now Reportable.—The reporting of occupational diseases is now required by law in Kentucky, according to *Industrial Medicine*. Thirty-four diseases in this classification have been "declared dangerous to the public health," it was stated.

Doctors Day.—Doctors Day, honoring all members of the medical profession in Kentucky, will be observed by the woman's auxiliary to the Kentucky State Medical Association on April 13, giving special recognition to Dr. William A. McDowell, Cynthiana, author of "A Demonstration of the Curability of Pulmonary Consumption in All Its States—Comprising An Inquiry into the Nature, Causes, Symptoms, Treatment and Prevention of Tuberculosis Diseases in General." The book was published in Louisville by Prentice and Weissinger in 1843.

MASSACHUSETTS

Dr. Thorn Given Chancellor's Medal for Achievement.—At the recent graduation ceremonies of the University of Buffalo the chancellor's medal, awarded annually by the university council for outstanding achievement, was presented to Dr. George W. Thorn, Hersey professor of the theory and practice of physic in the Harvard Medical School and physician in chief of the Peter Bent Brigham Hospital, Boston.

New Health Officers.—Dr. Harold W. Stevens, Middleboro, was recently elected president of the Massachusetts Public Health Association to succeed Dr. Henry D. Chadwick, Waltham, who retired after two terms. Other officers include Drs. Lawrence Jackson Smith, Springfield, and Charles F. Wilinsky, Boston, vice presidents, and Raymond S. Patterson, Ph.D., who was chosen secretary to succeed G. Donald Buckner, S.B., Worcester, who retired on account of his removal to Worcester to become secretary of the Southern Worcester County Health Association. Mr. Buckner had held the secretaryship since 1934

MICHIGAN

Personal.—William J. Burns, LL.B., executive secretary of the Michigan State Medical Society, Lansing, has been appointed a member of the public relations committee of the State Bar of Michigan.——Dr. Wilfrid Haughey, Battle Creek, has been elected editor of the *Journal* of the Michigan State Medical Society, succeeding Dr. Ray H. Holmes, Muskegon, who has entered army service.

Changes in Health Personnel.—Dr. N. Berneta Block, Lansing, a member of the staff of the state department of health since 1937, has been named director of the Alger-Schoolcraft health department with headquarters in Manistique. Dr. Block succeeds Dr. Jean B. Ruhl-Koupal, who has been named director of health district number one including Crawford, Kalkaska, Missaukee and Roscommon counties.

Motor Vehicles Lead Accidental Deaths.—Motor vehicles accounted for 1,295 deaths in 1942 out of the total of 3,591 accidental deaths for Michigan as a whole. Although leading the list of accidental deaths, this is the smallest total in this group in the last nine years. Accidents in the home were second in the list of causes with a total of 1,254 deaths. According to an announcement from the state department of health, 366 occupational deaths are listed in the accidental death summary as follows: manufacturing 94, agricultural 81, transport and public utilities 47, extractive industries (others than mining and quarrying) 28, construction 22, mining and quarrying 19, trade 18, clerical and professional service 3 and all others 54.

MISSOURI

State Medical Meeting.—The Missouri State Medical Association will hold its annual session in St. Louis, April 18-20, under the presidency of Dr. Homer L. Kerr, Crane. The preliminary program includes the following discussions: the sulfonamides by Drs. Henry L. Barnett, St. Louis, and Walter S. Sewell, Springfield; burns by Drs. Robert Elman, St. Louis, Francis T. H'Doubler, Springfield, and Earl C. Padgett, Kansas City; poliomyelitis by Lloyd R. Jones, Ph.D., St. Louis, Drs. John Albert Key, St. Louis, and Damon O. Walthall, Kansas City; industrial medicine as related to physical examination and industrial hazards by Dr. Edwin C. Funsch, St. Louis; syphilis by Drs. Joseph F. Bredeck and Arthur W. Neilson, St. Louis; anesthesia by Drs. Joseph A. McNearney, St. Louis, and Paul H. Lorhan, Kansas City; respiratory disease by Drs. Robert A. Moore and Henry Pinkerton, St. Louis, and a discussion on transfusions by Drs. Carl V. Moore and Raymond O. Muether, St. Louis.

NEW YORK

Teaching Day on Chemical Warfare.—A teaching day for physicians and nurses on "Medical Aspects of Chemical Warfare" will be held at Syracuse University College of Medicine, April 9. Consisting of a three hour review session with discussion of new developments, the instruction will be presented by the college of medicine in cooperation with the health preparedness commission of the state war council, the Medical Division of the Office of Civilian Defense and the state department of health.

Commissioner of Mental Hygiene Resigns.—Dr. William J. Tiffany, Albany, has resigned as commissioner of mental hygiene, effective April 1. A graduate of Columbia University College of Physicians and Surgeons, Dr. Tiffany has been in charge of the state department of mental hygiene since 1937. He entered the state hospital service in 1906 and served on the staffs of the Binghamton State Hospital, Binghamton, the Manhattan State Hospital, New York, and the Kings Park State Hospital, Kings Park, of which he was made superintendent in 1926. In 1931 he was appointed head of the Pilgrim State Hospital, Brentwood.

Program on Plasma Therapy and Blood Transfusion.—Plans have been completed to present to the medical profession of the state the latest information on blood therapy and whole blood transfusion under the auspices of the state medical society, the Office of Civilian Defense, the Health Preparedness Commission of the State War Council and the state department of health. Expenses of the speakers are to be paid by the state medical society and the state department of health. The lectures may be arranged as special single sessions or in connection with formal courses or for a special or regular meeting of county medical societies. The physicians available for lectures and demonstrations attended a meeting on February 26 in the State Office Building, Albany, to hear discussions on plasma therapy and whole blood transfusion.

New York City

The Seventh Harvey Lecture.—Dr. Oswald H. Robertson, professor of medicine, University of Chicago School of Medicine, will deliver the seventh Harvey Society Lecture of the current series at the New York Academy of Medicine on April 15. His subject will be "Sterilization of Air with Glycol Vapors."

Navy Officers Study Hygiene to Protect Workers.—A group of naval officers are studying industrial hygiene for the protection of civilian workers in shipyards, arsenals and other naval stations at the De Lamar Institute of Public Health, Columbia University College of Physicians and Surgeons. The sixteen medical officers will train for three months at Columbia. The course will include the study of the causes of absenteeism, occupational skin diseases, ventilation and temperature, and the hazards present in toxic volatile materials in the manufacture of explosives.

Postgraduate Courses.—The Long Island College of Medicine and the Medical Society of the County of Kings, Brooklyn, opened a spring program of postgraduate courses in March. Subjects covered by the series include regional anesthesia, allergy, clinical cardiology, electrocardiography and clinical cardiology, gastroenterology, diseases of the peripheral blood vessels, peripheral vascular diseases, diabetes, hypertension and nephritis, female sex endocrinology, gynecologic pathology, endocrine diseases and disorders in children and adolescents, diseases of children, cardiovascular roentgenology, x-ray diagnosis, fractures, proctology and urology.

VIRGINIA

Annual Spring Graduate Course.—The Gill Memorial Eye, Ear and Throat Hospital, Roanoke, will conduct its seventeenth annual spring graduate course in ophthalmology, otology, rhinology, laryngology, faciomaxillary surgery, bronchoscopy and esophagoscopy, April 5-10. Among the speakers will be:

Dr. Theodore E. Walsh, St. Louis, Prophylaxis and Treatment of Upper Respiratory Infections.
Dr. John R. Lindsay, Chicago, Management of Acute Suppuration in the Middle Ear and Petrous Pyramid, Including Common Complications.
Rear Admiral Luther Sheldon Jr., medical director, U. S. Navy, Washington, D. C., Relationship of Otolaryngology to Naval Medicine.
Dr. Perry G. Goldsmith, Toronto, Commentary on the Relationship Between Accessory Sinus Diseases and General Medicine.
Lieut. Comdr. Charles H. Best, R. C. N. V. R., Toronto, Physiology in War Medical Research.
Dr. John R. Richardson, Boston, Applied Anatomy of the Head and Neck.
Dr. French K. Hansel, St. Louis, Diagnosis of Allergy of the Nose and Paranasal Sinuses.
Dr. Albert A. Cinelli, New York, Treatment of Recent Fractures of the Nose and Fractures Extending into the Maxillary Accessory Sinuses.
Dr. F. Bruce Fralick, Ann Arbor, Mich., Surgical Anatomy of the Eye and Adnexa.
Dr. Peter C. Kronfeld, Chicago, Classification of Glaucoma.
Dr. George P. Guibor, Chicago, Physiologic Principles Used in the Diagnosis of Motor Disturbances and Their Practical Applications.
Dr. John M. McLean, New York, Intraocular Tumors and Recent Advances in Their Treatment.
Dr. Robert J. Masters, Indianapolis, Practical Application of Slit Lamp Microscopy in Routine Practice of Ophthalmology.
Dr. Albert L. Brown, Cincinnati, Ocular Therapeutics.
Dr. Ramon Castroviejo, New York, Lid Surgery.
Dr. Willis S. Knighton, New York, Refraction: Routine Procedures.

The annual banquet will be held at the Hotel Roanoke, Tuesday, April 6, with an address by Drs. James A. Babbitt, Philadelphia, and Warren F. Draper, assistant surgeon general, U. S. Public Health Service, Washington, D. C., on "Problems of Current Interest in Public Health and Medical Care for the Civilian Population."

WISCONSIN

Registry of Tropical and Exotic Diseases.—Dr. Harry Beckman, professor of pharmacology, Marquette University School of Medicine, Milwaukee, is working on the establishment of a registry of all cases of tropical and exotic diseases such as malaria, Weil's disease, filariasis, relapsing fever, giardiasis, strongyloides dysentery, fluke and rare worm infections, histoplasmosis and endemic flea borne typhus. Any physician reporting such cases to Dr. Beckman will be given credit, the information to be placed in the archives of the American Society of Tropical Medicine and prepared as a compilation of cases for Wisconsin.

Industrial Clinic.—The second postgraduate industrial, medical and surgical clinic will be held at the Loraine Hotel, Madison, May 5, and at the Conway Hotel, Appleton, May 6. "Keep 'em Working" is the theme of the clinic as it was for the first one held last November. In addition to the scientific program which has been arranged for physicians, a special

program has been arranged for employers, nurses, personnel directors and others interested in industrial health problems. The clinic is sponsored by the council on scientific work and the committee on industrial health of the state medical society and the industrial hygiene unit of the state board of health.

Distinguished Service Pin Awarded to State Cancer Commander.—Mrs. G. E. Stoddart, Beaver Dam, regional deputy commander and state commander of the Wisconsin division of the Women's Field Army of the American Society for the Control of Cancer, was presented with the society's distinguished service pin during its recent meeting in New York. The decoration, which was given for outstanding service during the previous year in the cause of cancer control, is presented annually. Mrs. Stoddart is the second Wisconsin woman to be so honored. Mrs. Frederick H. Clausen, Horicon, was awarded the pin in 1939 in recognition of her efforts in establishing the *Bulletin* of the Women's Field Army of Wisconsin.

GENERAL

Dental Association Moves.—The American Dental Association has moved into a new five story building at 222 East Superior Street, Chicago.

Journal of Aviation Medicine.—With the beginning of volume 14 (February issue) the *Journal of Aviation Medicine* will be published six times a year instead of four.

Dr. Weed Named Chairman of Red Cross Advisory Committee.—Dr. Lewis Hill Weed, professor of anatomy, Johns Hopkins University School of Medicine, Baltimore, has been made chairman of the Medical and Health Advisory Committee of the American Red Cross.

Hospital Standards Bureau Publishes Service Bulletin.—The Hospital Bureau of Standards and Supplies, New York, brought out a new monthly service bulletin in January called the *Bureau News*. The first issue contains announcements concerning threatened food shortages, frozen and dehydrated foods, coffee stretchers and point rationing, discussions on various hospital necessities and consideration of miscellaneous subjects of interest to buyers and managers.

Women's Work Clothes Standardized.—The American Standards Association has been requested by the Office of Price Administration to initiate a war project to standardize women's work clothes. The request carries the endorsement of the War Production Board and seeks among other things a standard to protect the workers adequately against specific occupational hazards, thus preventing accidents and reducing absenteeism resulting from accidents.

Cancer Control Month.—President Roosevelt has designated the month of April as "Cancer Control Month" and, in his proclamation on March 22, called on the governors of states, territories and possessions to authorize local observances. The President also asked the medical profession, schools and colleges, press, radio, motion picture industry and all agencies and individuals interested in a national campaign for the control of cancer to spread the knowledge of the early symptoms of the disease and to publish information about the location and function of clinics and other health facilities engaged in the warfare on cancer.

Survey Shows Opposition to Hospital Plan.—Results of a survey completed by *Hospital Management* reveal overwhelming opposition to the proposed expansion of the Social Security plan to cover hospitalization and a corresponding opinion that the voluntary "Blue Cross" plans can meet the need for hospital insurance. According to *Hospital Management* the survey shows a strong vote in favor of expanding the Social Security old age and survivorship benefits to cover hospital employees and a considerable majority in favor of federal aid to the states for the hospitalization of the indigent as preferable to a federally operated hospitalization plan. The survey indicates that "the doors of the hospital are open to all, regardless of the ability of the patient to pay and regardless of the fact that approximately one out of eight localities has no form of aid to the hospital for such cases. In 7 out of 8 cases some form of aid, ranging from tax supported hospitals to payment of a part of the cost to voluntary hospitals, is provided for the care of the indigent sick."

Response to Requests for Parasitological Specimens.—The Distributing Center for Parasitological Specimens, formed under the auspices of the National Research Council and the Association of American Medical Colleges in October 1942, wishes to acknowledge the cooperation displayed by various institutions in sending specimens. Considerable material has been forwarded to the center and is being redistributed to the various medical schools teaching tropical medicine and parasitology in accordance with their requests. The center is located at the Army Medical School, Army Medical Center, Washington, D. C., and is operated by the school's department of parasitology and tropical medicine. The center was set up as a collecting and distributing agency for gross and microscopic specimens of value to medical schools needing additional material for the teaching of tropical medicine. The center wishes to acknowledge the following institutions, departments and/or individuals for their generous cooperation in supplying much needed material:

Medical Schools

Baylor
California
Chicago
Columbia
Indiana
Maryland
Minnesota
Missouri
New York Univ.
Tennessee
Yale

Zoology Departments

U. of Calif. at Los Angeles
Iowa State
Johns Hopkins
Michigan
Pennsylvania
Rice Institute
Tulane

General Hospitals

Letterman

Station Hospitals & Service Command Labs.

Puerto Rican Dept. Lab.
4th Service Command Lab.

Other

Army Medical Museum
Dept. of Parasitology, AMS
Med. Dept. Prof. Service Schls., AMC
Virus Lab., AMS
Board of Health Lab., Canal Zone
Bureau of Animal Industry
National Institute of Health
New York Public Health Service
U. S. Public Health Service

More than 1,200 items had been shipped to fifty-seven institutions on February 12. All shipments are sent as gifts. Major George W. Hunter III, sanitary corps, U. S. Army, is in charge of the Distributing Center for Parasitological Specimens.

Activities of Nutrition Foundation.—The Nutrition Foundation, Inc., has authorized grants totaling $148,550, including $110,700 for the renewal of twenty-eight projects supported by the foundation during 1942 and $37,850 for fifteen new research projects. The announcement followed a meeting of the board of trustees at the Waldorf-Astoria Hotel, New York, March 12. The foundation has given $316,000 in research grants to forty universities since its organization a year ago. Institutions which received new grants were the University of Wisconsin, Madison; Harvard University, Cambridge, Mass.; University of Toronto; Columbia University, New York; University of California, Berkeley; Johns Hopkins University, Baltimore; New York University; Massachusetts State College, Amherst; University of Chicago; Yale University, New Haven; Cornell University, Ithaca; Oregon State College, Corvallis, and Oklahoma Experiment Station, Stillwater. Oliver C. Carmichael, LL.D., chancellor of Vanderbilt University, Nashville, Tenn., and Dr. Frank G. Boudreau, New York, executive director of the Milbank Memorial Fund and vice chairman of the Committee on Food and Nutrition of the National Research Council, were chosen public members of the foundation, and Dr. Virgil P. W. Sydenstricker, Augusta, professor of medicine, University of Georgia School of Medicine, was appointed a member of the scientific advisory committee. The Container Corporation of America, Chicago, and the Pillsbury Flour Mills, Minneapolis, were elected founder members. The National Sugar Refining Company, New York, P. Duff & Sons, Pittsburgh, R. B. Davis Company, Hoboken, N. J., and the Curtiss Candy Company, Chicago, were elected sustaining members. New members of the board of trustees, representing the new members of the foundation, were announced as follows: Ellsworth Bunker, president, National Sugar Refining Company; Walter P. Paepcke, president, Container Corporation of America; William H. Duff II, president, P. Duff & Sons, Inc.; B. E. Snyder, treasurer, R. B. Davis Company; Philip W. Pillsbury, president, Pillsbury Flour Mills Company, and Otto Y. Schnering, president, Curtiss Candy Company. Among the more important studies in which progress has been made is one carried on by William C. Rose, Ph.D., of the University of Illinois, Urbana, and bearing on the human requirement of amino acids, the "building blocks of proteins," which occur in such foods as milk, meat, eggs and fish. Coincident with Dr. Rose's work showing specific amino acids to be essential in human nutrition, Vincent du Vigneaud, Ph.D., Cornell University Medical College, New York, has clarified some of the important functions of amino acids in the human body, following earlier studies on the effects of these same acids on experimental animals. Other studies in which excellent progress has been made include the problem of supplying fats to the armed forces in all sections of the world, on nutrition problems relating to aviation and desert warfare, and on the effect of extremes of environment on nutritional requirements.

Foreign Letters

LONDON LETTER

(From Our Regular Correspondent)

Feb. 20, 1943.

Stamping Out of an Imported Outbreak of Smallpox

Smallpox has been stamped out of this country, but cases arrive from time to time from other countries. A ship from Bombay and Capetown docked on May 29 at Glasgow with 1,000 passengers and 200 crew. A sick engineer was found to have confluent smallpox which proved fatal. All on board were immediately vaccinated, but on June 23 another 7 of the crew, 2 passengers and a contact medical officer had developed the disease. This was disappointing, for in 5 of the cases vaccination must have been done early in the incubation period—between the first and fifth days—when it usually confers protection. On the other hand, smallpox did not attack any of the 163 members of the crew who had been vaccinated on a previous voyage in 1940. Of those attacked 1 was a Polish officer who had been vaccinated nine years previously for the third time, while the medical officer, aged 34, had been vaccinated in infancy. The other 8 had never been vaccinated.

The sequel was alarming. From June 26 onward, cases of smallpox cropped up in different parts of Glasgow without any apparent connection with the ship or with one another. At first only the usual precautions were taken; contacts and neighbors were kept under surveillance and were offered vaccination so as to form a cordon of protected persons round each focus of infection. But the foci multiplied and the situation was deemed so serious as to require vaccination on a large scale. Twenty-five vaccination stations were opened, to which 282,255 persons came in the first week of July. Including those attending private physicians, it is believed that half a million were vaccinated during the month.

In view of the virulence of the infection, which was fatal in 6 out of 25 cases, the usual single stroke method of vaccination was abandoned for three strokes ⅜ inch long and ⅛ inch apart. It was also felt that unless there was a history of recent vaccination a single unsuccessful attempt should not be taken as evidence of immunity, and vaccination was repeated if no reaction was seen within four days. These comprehensive measures were successful. The 21 apparently primary cases gave rise to only 4 secondary ones and by July 31 the outbreak had ceased.

The Glasgow health officer points out that much would be gained if ships' doctors could diagnose smallpox at once and vaccinate all on board. But it is still better to immunize before the disease breaks out, and he holds that all passengers and crews from Eastern ports should be vaccinated as a condition of travel.

American War Blinded to Be Cared for at St. Dunstan's

The institute for those blinded in the war known as St. Dunstan's was founded twenty-five years ago by Sir Ian Fraser, who was blinded in the first world war and has presided over its activities ever since. His recollection is that fear of blindness is the worst part of eye injuries. It is an economic fear and a fear of loneliness and dependence. To avoid this reaction any one whose eyes are seriously damaged should go to St. Dunstan's, which is a training center where they will see others who have overcome the handicap of blindness incurred in the first world war. They act as instructors in braille, typewriting, shorthand, massage, joinery and other handicrafts. Living in a world of the blind, the newcomers soon begin to concentrate on the things they can do and forget the things they cannot do. They are amazed at the variety of occupations open to the blind. They quickly learn to read, write and get about by themselves. Not all those admitted become blind. St. Dunstan's has a hospital, and half the patients admitted have left after a few months treatment with vision sufficiently restored to go back to military or civil life. St. Dunstan's has, with the consent of the German authorities and with the help of the Red Cross, established a school in Germany for blinded British prisoners of war. It has been arranged that American blinded in the war are to be admitted to St. Dunstan's.

In a luncheon at St. Dunstan's Sir Ian Fraser said that in this war, presumably owing to the increased use of armor in tanks and planes, fewer men were blinded by fragments of metal than in the last war. But a larger proportion were blinded by concussion causing collapse of the eye or irreparable damage from hemorrhage. About 288 had come under the care of St. Dunstan's in this war. Of these 88 had recovered some useful sight and 200 would not recover any sight at all. Of the 200, half are being trained or have been trained at St. Dunstan's and 30 are in Germany as prisoners of war. It has been arranged that all American soldiers who may be temporarily or permanently blinded shall be sent to St. Dunstan's for three to six weeks while awaiting to return home. Brig. Gen. Paul Hawley, chief surgeon of the United States Army in the European theater of operations, said that the great shock to the blinded American soldier would come when he returned home handicapped and helpless to his family. Now he would be able to return after his St. Dunstan's training walking with confidence and facing the world with courage.

Annual Congress of Ophthalmological Society

Another illustration of the fact, shown in previous letters, that we do not allow the war to interfere with normal activities when they do not impair our fighting powers is shown by the holding of the annual congress of the Ophthalmological Society in London, which will be held on April 30 and May 1. Discussions will take place on "Thyrotoxicosis in Its Relation to Ophthalmology," to be opened by Dr. Russell Brain and Mr. H. L. Savin, and on "The Scientific and Clinical Aspects of Night Vision," to be opened by Prof. W. J. B. Riddell and Air Commodore P. C. Livingstone.

Men with Amputations in German Prison Camps

The temporary artificial limbs supplied by the Germans to British prisoners were found to be badly fitting. For a time the Red Cross sent limbs by post in response to measurements. This was not successful, so last year it obtained permission to visit the camps and make a survey. Swiss orthopedic specialists were sent and worked out every detail for 430 men. They suggested that a new set of limbs should be made by Swiss experts, who would visit the camps and fit them. This is being done.

New Appointment for Professor Ryle

Dr. J. A. Ryle, regius professor of physic, University of Cambridge, has been elected professor of social medicine at Oxford.

Marriages

JAMES W. CHAMBERS, Fort Riley, Kan., to Miss Mollie Bauman of Des Moines, Iowa, in Whittemore, Iowa, February 4.

RUDOLPH MATAS LANDRY, New Orleans, to Miss Jane Eleanor Willius of Rochester, Minn., February 27.

HOWELL HOOD SHERROD, Johnson City, Tenn., to Miss Alice E. Simpson at Strawberry Plains, February 26.

THOMAS NOBLE WARREN, Wilmington, Del., to Miss Jean Duncan Drysdale of Lynchburg, Va., March 1.

PIERRE FABIAN LA BORDE JR., Columbia, S. C., to Miss Virginia Adams of Charleston in March.

JOHN RANDOLPH KIGHT, Norfolk, Va., to Miss Nancy Pearis Edgar of Charlottesville, March 6.

GUY O. PFEIFFER, O'Fallon, Ill., to Miss Mary Kathryn Kubitschek of St. Louis, March 9.

Deaths

Charles **Francis Yerger,** Chicago; Ph.G., Northwestern University School of Pharmacy, Chicago, 1898; M.D., Northwestern University Medical School, Chicago, 1905; member of the Illinois State Medical Society; in 1930 joined the faculty of Loyola University School of Medicine as a clinical instructor in ophthalmology and later became an associate clinical professor of ophthalmology; formerly instructor in medicine, instructor in operative surgery, instructor and associate in laryngology, rhinology and otology at the University of Illinois College of Medicine; instructor in otolaryngology at Rush Medical College, 1912-1913; specialist certified by the American Board of Ophthalmology and the American Board of Otolaryngology; member of the Chicago Otolaryngological Society and the Chicago Ophthalmological Society; for many years on the staff of the Illinois Charitable Eye and Ear Infirmary; attending physician to the Juvenile Detention Home and Juvenile Court since 1914; served as attending otolaryngologist and ophthalmologist to the Cook County Hospital, attending ophthalmologist to the Chicago State Hospital and the Lutheran Memorial Hospital; on the staff of the Hospital of St. Anthony de Padua; a medical examiner of the Cicero Selective Service Board, 1917-1918; aged 63; died, March 16, of uremia and hypertension.

Ezra Kimball Sprague ✠ Medical Director, U. S. Public Health Service, retired, Brooklyn; College of Physicians and Surgeons, Boston, 1890; joined the U. S. Public Health Service as an assistant surgeon in 1893, was promoted through the various ranks and retired in 1932 with the title of medical director; served in various posts in the United States, at Antwerp, Belgium, and Calcutta, India; professor of tropical medicine at the Detroit Medical College, 1901-1902; studied bubonic plague in Calcutta, 1903-1904; chief medical officer at Ellis Island from 1925 to 1928 and a director of the North Atlantic district of the Public Health Service from 1928 to 1932; in charge of extra cantonment zone sanitation at Camp Devens, Ayer, Mass., and Camp Dodge, Des Moines, Iowa, during World War I; made reports on drinking water which resulted in the installation of a filtration plant at Washington, D. C., in 1898; aged 76; died, February 2, of carcinoma of the colon.

Franklin Paradise Johnson ✠ Portland, Ore.; Johns Hopkins University School of Medicine, Baltimore, 1920; assistant clinical professor of urology at the University of Oregon Medical School; from 1908 to 1910 Austin teaching fellow at Harvard Medical School, Boston, and instructor of histology and embryology from 1910 to 1912; assistant professor of anatomy in 1912, associate professor in 1913 and professor 1919-1920 at the University of Missouri, Columbia; specialist certified by the American Board of Urology, Inc.; member of the American Urological Association and the American Association of Anatomists; fellow of the American College of Surgeons; received the Ph.D. degree from Harvard University, Boston, in 1912; collaborator in the writing of a number of medical books; member of the staffs of the Multnomah Hospital and the Good Samaritan Hospital, where he died, February 12, of coronary thrombosis, aged 55.

John Frank Fraser ✠ New York; Bellevue Hospital Medical College, New York, 1892; specialist certified by the American Board of Dermatology and Syphilology; member of the American Academy of Dermatology and Syphilology; formerly assistant professor of clinical medicine (dermatology), Cornell University Medical College, and associate professor of clinical dermatology and syphilology at the New York Post-Graduate Medical School, Columbia University; served as a major in the medical corps of the U. S. Army during World War I; an associate attending physician in dermatology, New York Hospital; aged 75; died, January 31, in the French Hospital of pulmonary embolism following an appendectomy.

Elwood Tracy Easton ✠ Boston; Harvard Medical School, Boston, 1899; specialist certified by the American Board of Ophthalmology; member of the New England Ophthalmological Society; professor emeritus of ophthalmology at the Tufts College Medical School, where he served as professor and instructor of ophthalmology; for some time consulting oculist to the Parental School in West Roxbury; served as consulting surgeon in ophthalmology, ophthalmic surgeon and on the outpatient staff of the Massachusetts Eye and Ear Infirmary; for many years a trustee of the Gordon College and of the Baptist Home of Massachusetts; aged 66; died, January 31, of angina pectoris and arteriosclerosis.

Charles Shorey Butler ✠ Boston; Harvard Medical School, Boston, 1898; treasurer of the Massachusetts Medical Society; for many years assistant in anatomy at his alma mater; served for seven years as assistant surgeon in the Massachusetts Volunteer Militia and later as a captain and assistant surgeon in the Eighth Infantry Regiment; was made a Chevalier of the Legion of Honor by the French government for his service in the French Army; lieutenant colonel in the medical reserve corps of the U. S. Army not on active duty; served during World War I; aged 72; died, February 23, of coronary disease.

George Wilder Appleby, Waterloo, Iowa; Chicago Medical College, 1885; aged 82; died, January 22, of coronary occlusion.

William Thomas Bailey, Boston; Harvard Medical School, Boston, 1900; member of the Massachusetts Medical Society; past president of the Boston Anesthesia Society; aged 73; died, January 16, in the Massachusetts General Hospital, Phillips House, following an operation for carcinoma.

Charles Stephen Bartholomew Cassasa ✠ New York; Columbia University College of Physicians and Surgeons, New York, 1912; for many years instructor of pathologic anatomy at the Cornell University Medical College; an assistant medical examiner for the City of New York from 1918 to 1930; surgical director and chairman of the medical board of the Harlem, Lutheran, Mother Cabrini, St. Elizabeth and Knickerbocker hospitals; aged 57; died, February 22, of coronary thrombosis.

Gilbert de Leverance Forbes ✠ Kendall, N. Y.; University of Buffalo School of Medicine, 1909; for thirty years health officer of Kendall and school physician at the Kendall High School for twenty-five years; past president of the New York Association of School Physicians; aged 61; died, February 10, of heart disease and hyperthyroidism.

Thomas Jonathan Long ✠ Denison, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1902; fellow of the American College of Surgeons; mayor of Denison; formerly president of the Chamber of Commerce; served as chief of staff of the Missouri, Kansas, Texas Railroad Employees' Hospital and the Long-Sneed Clinic Hospital; aged 68; died, January 10, in Whitesboro of angina pectoris.

Paul Otto Luedeke, Rochester, N. Y.; University of Buffalo School of Medicine, 1901; member of the Medical Society of the State of New York; aged 73; died, January 25, of coronary occlusion and arteriosclerosis.

Clarence J. Stanley, Camp Wood, Texas; State University of Iowa College of Medicine, Iowa City, 1902; aged 69; died, January 9, of heart disease.

Wilson E. Van Loon, Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1891; aged 76; died recently in the Presbyterian Hospital of arteriosclerotic cardiovascular renal disease.

Frederick George Vogel ✠ Waterloo, Ill.; St. Louis University School of Medicine, 1906; aged 74; died, January 30, in St. Louis.

Hugh S. White ✠ El Paso, Texas; University College of Medicine, Richmond, 1900; past president of the El Paso County Medical Society; fellow of the American College of Surgeons; served on the board of health of El Paso County for many years and as city and county health officer; member of the staff of the El Paso Masonic Hospital, Hotel Dieu, Sisters' Hospital and the Southwestern General Hospital; on the board of the El Paso City-County Hospital; aged 67; died, January 22, of heart disease.

DIED WHILE IN MILITARY SERVICE

Arthur Pickens Vandergrift Jr., Memphis, Tenn.; University of Tennessee College of Medicine, Memphis, 1939; member of the Mississippi State Medical Association; served as director of the De Soto County health unit at Hernando, Miss.; began active duty as a first lieutenant in the medical corps, Army of the United States, and later became a captain; aged 28; was killed in an army bomber crash near Columbia, S. C., January 27.

T. Dwight Hunt, Madison, Wis.; University of Oregon Medical School, Portland, 1935; member of the State Medical Society of Wisconsin; was called to active duty in September 1942 as a first lieutenant in the medical corps, United States Army Air Corps; aged 35; stationed at Pueblo, Colo., where he was killed in an airplane accident, January 24.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

BOARDS OF MEDICAL EXAMINERS
BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL, March 20, page 974.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Various centers having 5 or more eligible applicants, June. Sec., Dr. J. S. Rodman, 225 S. 15th Street, Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF OPHTHALMOLOGY: *Parts I and II.* New York City, June 4-5, October 8-9. Sec., Dr. John Green, 6830 Waterman Blvd., St. Louis.

AMERICAN BOARD OF PATHOLOGY: Chicago, June 2-3. Final date for filing application is April 15. Sec., Dr. F. W. Hartman, Henry Ford Hospital, Detroit.

AMERICAN BOARD OF PEDIATRICS: *Written.* Locally, Oct. 8. *Oral.* New York, Nov. 20-21. Final date for filing application is Aug. 1. Starting July 1, 1943, Group I will be abolished. Sec., Dr. C. A. Aldrich, 707 Fullerton Ave., Chicago.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Medical Practice Acts: Unlicensed Practice by Chiropractor.—The defendant, a chiropractor, was convicted of practicing "chiropractic and medicine" in Virginia without the license required by law and appealed to the Supreme Court of Appeals of Virginia, which reversed and remanded the case (*Grosso* v. *Commonwealth*, 177 Va. 830, 13 S. E. (2d) 285; J. A. M. A. **116**:2103 [May 3] 1941). He was again tried and convicted and again appealed to the Supreme Court of Appeals of Virginia.

The defendant contended, among other things, that the evidence adduced at the trial was not sufficient to sustain the conviction. It appeared from the evidence that he had rented rooms in an office building and had fitted them out with appropriate appliances. He had a secretary, and he listed himself as a chiropractor in the local telephone book and by publications kept the public advised of his movements. Furthermore, the defendant held himself out as being competent to treat a wide variety of cases, extending from backache to heart disease, and he published testimonials to the effect that he could and did cure disorders which did not yield to conventional treatment. On the basis of this evidence the court held that the verdict was plainly supported.

It was next contended that the trial court erred in admitting evidence tending to show the conduct of the defendant immediately before Dec. 11, 1939, which was the date on which it was charged that the chiropractor violated the medical practice act. Of course, said the court, the commonwealth must prove, and it did prove, that he violated the medical practice act. If Dec. 11, 1939 had been curtained off, the jury could not have told what it was all about. When the defendant set himself up in business and held himself out as a chiropractor, without having obtained a license to follow that vocation, his offense was a continuing one. Accordingly, evidence of his conduct immediately prior to Dec. 11, 1939 was admissible in evidence.

Finally, it was contended that the defendant and his school of medicine were discriminated against in that chiropractic was not recognized in the medical practice act as a worth while school of the healing art. The chiropractor's approach is wrong, said the court. The chiropractor's real complaint is that no special provision is made in the medical practice act for him. A chiropractor can be licensed to practice when he meets the requirements of the board of medical examiners. Under the provisions of the medical practice act, an applicant to be licensed must show that he has studied medicine not less than four school years, including four satisfactory courses of at least eight months each in four different calendar years in a medical school registered as maintaining a standard satisfactory to the state board of education. The defendant, it appeared, had graduated from the Palmer School (a full three year course) at which school was taught "a course of anatomy, histology, physiology, embryology, and chemistry." The defendant had not applied to the board of medical examiners for a certificate, and with no training other than what he possesses he could not have applied successfully. Statutes designed to preserve the people's health must be very arbitrary to be unconstitutional. New schools must prove their worth to the satisfaction of the legislature before they are recognized. They come and go and "continue not in one stay." It is within wide limits for the legislature to say when their worth has been sufficiently established and what are the tests they must undergo. Certainly, the court concluded, the science of medicine is not static; but society must protect itself against those who are unable or unwilling to undergo that training and to measure up to those requirements now fairly universally recognized. Accordingly the judgment of conviction was affirmed.—*Grosso v. Commonwealth, 21 S. E. (2d) 728 (Va., 1942).*

Medical Practice Acts: Unlicensed Practice as Violation of Act in Absence of Express Prohibition Against Unlicensed Practice.—Miller, a chiropractor, was convicted of unlawfully practicing medicine in Virginia in violation of the medical practice act of that state in that he had not taken and passed the examination which persons who desire to practice medicine in Virginia must take and pass before the Virginia state board of medical examiners. He appealed to the Supreme Court of Appeals of Virginia, contending that no statute in Virginia required him to take and pass an examination before the board of medical examiners as a condition precedent to the practice of medicine.

In passing on the validity of the chiropractor's contention, it was necessary for the court to consider the legislative history of the laws regulating the practice of medicine in the state. Briefly, the first medical practice act enacted in Virginia was enacted in 1884 (Acts of Assembly, 1883-84, p. 79), and that act contained a specific section (seven) which, in effect, prohibited any person who commenced the practice of medicine after Jan. 1, 1883, from practicing for compensation "without first having obtained a certificate" from the board of medical examiners. In 1912 the 1883 act and the amendments thereto were repealed and a completely new medical practice act was adopted. That new act provided for a board of medical examiners to examine and license applicants for licenses to practice medicine. Provision was made for "legal practitioners of medicine practicing under the provisions of previous laws." The board was given authority, in its discretion, to arrange for the issuance of licenses by reciprocity. The board was authorized for stated causes to refuse to examine applicants or to revoke or suspend licenses already issued. A section denominated certain classes of persons who were exempt from the provisions of the act under stated circumstances. Licentiates who were graduates of sectarian schools were not permitted to administer drugs or practice surgery unless authorized to do so by the board. The penalty section merely provided that any person practicing medicine in the state in violation of the act should be subjected to a certain penalty. The act was amended from time to time but in no way material for the purposes of the present discussion. In 1942 the legislature killed a bill which would

have amended the medical practice act so as specifically to make it unlawful for any person to engage in the practice of medicine in the state without first having obtained from the board of medical examiners a license or certificate to do so. The gist of the chiropractor's argument was that since the medical practice act of 1912, as amended, did not specifically prohibit practice without complying with the provisions of the act—that is, with respect to a person not entitled to reciprocity or not exempted from the act—without first submitting to and passing an examination by and being licensed by the board of medical examiners, no penalty could be imposed on a person who practices medicine without submitting to and passing an examination and being licensed by the board of medical examiners.

The original medical practice act, said the Supreme Court of Appeals, specifically made it unlawful for a person to commence the practice of medicine or surgery after Jan. 1, 1883 for compensation without first having obtained a certificate from the board of medical examiners. Plainly the medical practice act of 1912, which repealed the prior act, was intended to regulate properly the practice of medicine and surgery. The necessity for regulation is made plain by the fact that the act was an emergency act. It was intended to put up bars and not let them down. Conditions under which certificates might be obtained were made more stringent. If the chiropractor's contention is sustained, then the net effect of the 1912 act was to make the suppression of incompetent followers of the healing art impossible. To attribute to that act any such purpose is unthinkable. If the contention of the chiropractor with respect to the 1912 act, as amended, is sound, then any one, at his election, be he snake doctor or magician, can hold himself out as a qualified practitioner of medicine and follow that vocation; all the trouble that the legislature has taken to safeguard the profession and to make an efficient aid to public health is but a futile gesture. As was said by the Supreme Court of Appeals of West Virginia in *Newhart* v. *Pennybacker*, 120 W. Va. 774, 200 S. E. 350:

> Where a particular construction of statute will result in an absurdity, some other reasonable construction which will not produce the absurdity will be made.

The 1912 statute, which became a law thirty years ago, continued the court, has been everywhere construed as the Commonwealth contends that it should be construed as prohibiting unlicensed practice. That construction which for a long period of time has been accepted by bench and bar as the true construction of a statute becomes a canon of construction, unless some paramount reason is advanced for a change of the conclusion. *St. Joseph's Soc.* v. *Virginia Trust Co.*, 175 Va. 503, 9 S. E. (2d) 304. Again, the legislature has seen fit to except from the operation of the medical practice act stated types of physicians under stated circumstances. Such physicians are not required to secure certificates from the examining board under the circumstances stated. Such an exception would be wholly unnecessary if no one was obliged to secure a certificate. Again, authority is given the board in its discretion to arrange for reciprocity with the authorities of other states and territories having requirements equal to those established in Virginia. Obviously, no reciprocity would be necessary if anybody could practice medicine in the state. The legislature, continued the court, had occasion to consider this subject at its 1942 session when it had before it the bill previously referred to which specifically proposed to prohibit a person practicing in the state without being licensed to do so by the board of medical examiners. Since it refused to pass that bill, it must be presumed that it was not thought necessary to pass such a measure because the matters dealt with in the bill had theretofore been amply covered by the statute.

For the reasons stated, the judgment of conviction was affirmed.—*Miller v. Commonwealth, 21 S. E. (2d) 721 (Va., 1942).*

Society Proceedings

COMING MEETINGS

Alabama, Medical Association of the State of, Birmingham, April 20-22. Dr. Douglas L. Cannon, 519 Dexter Ave., Montgomery, Secretary.
American Association of Industrial Physicians and Surgeons, Rochester, N. Y., May 25-27. Dr. E. C. Holmblad, 28 East Jackson Blvd., Chicago, Managing Director.
American Association on Mental Deficiency, New York, May 12-15. Dr. Neil A. Dayton, Mansfield Training School, Mansfield Depot, Conn.
American Gastro-Enterological Association, Atlantic City, N. J., May 3-4. Dr. J. Arnold Bargen, 102 Second Ave. S.W., Rochester, Minn., Secretary.
American Neurological Association, New York, May 6-7. Dr. Henry A. Riley, 117 East 72d St., New York, Secretary.
American Psychiatric Association, Detroit, May 10-13. Dr. Winfred Overholser, St. Elizabeth's Hospital, Washington, D. C., Secretary.
American Psychoanalytic Association, Detroit, May 9-11. Dr. Leo H. Bartemeier, General Motors Bldg., Detroit, Secretary.
American Society for Clinical Investigation, Atlantic City, N. J., May 3. Dr. Wesley W. Spink, University Hospital, Minneapolis, Secretary.
American Surgical Association, Cincinnati, May 13-14. Dr. Warfield M. Firor, Johns Hopkins Hospital, Baltimore, Secretary.
Arizona State Medical Association, Tucson, April 30-May 1. Dr. Frank J. Milloy, 112 North Central Avenue, Phoenix, Secretary.
Arkansas Medical Society, Little Rock, April 19-20. Dr. W. R. Brocksher, 602 Garrison Ave., Fort Smith, Secretary.
California Medical Association, Los Angeles, May 2-3. Dr. George H. Kress, 450 Sutter St., San Francisco, Secretary.
Connecticut State Medical Society, New Haven, May 25-27. Dr. Creighton Barker, 258 Church Street, New Haven, Secretary.
Florida Medical Association, Jacksonville, April 15-16. Dr. Shaler Richardson, 111 West Adams St., Jacksonville, Secretary.
Georgia, Medical Association of, Atlanta, May 11-14. Dr. Edgar D. Shanks, 478 Peachtree St. N.E., Atlanta, Secretary.
Illinois State Medical Society, Chicago, May 18-20. Dr. Harold M. Camp, 224 South Main St., Monmouth, Secretary.
Iowa State Medical Society, Des Moines, April 29-30. Dr. Robert L. Parker, 3510 Sixth Avenue, Des Moines, Secretary.
Maryland, Medical and Chirurgical Faculty of, Baltimore, April 27-28. Dr. W. Houston Toulson, 1211 Cathedral St., Baltimore, Secretary.
Massachusetts Medical Society, Boston, May 24-26. Dr. Michael A. Tighe, 8 Fenway, Boston, Secretary.
Minnesota State Medical Association, Minneapolis, May 17-19. Dr. B. B. Souster, 493 Lowry Medical Arts Bldg., St. Paul, Secretary.
Mississippi State Medical Association, Jackson, May 11-13. Dr. T. M. Dye, Clarksdale, Secretary.
Missouri State Medical Association, St. Louis, April 18-20. Mr. Raymond McIntyre, 634 North Grand Blvd., St. Louis, Executive Secretary.
National Tuberculosis Association, St. Louis, May 5-6. Dr. Charles J. Hatfield, 7th and Lombard Sts., Philadelphia, Secretary.
New Hampshire Medical Society, Manchester, May 11. Dr. Carleton R. Metcalf, 5 South State St., Concord, Secretary.
New Jersey, Medical Society of, Newark, May 25-26. Dr. Alfred Stahl, 55 Lincoln Park, Newark, Secretary.
New York, Medical Society of the State of, Buffalo, May 3-6. Dr. Peter Irving, 292 Madison Ave., New York, Secretary.
North Carolina, Medical Society of the State of, Raleigh, May 10-12. Dr. Roscoe D. McMillan, Red Springs, Secretary.
North Dakota State Medical Association, Bismarck, May 10-11. Dr. L. W. Larson, 221 Fifth Street, Bismarck, Secretary.
Northern Tri-State Medical Association, Ann Arbor, Mich., April 13. Dr. F. R. Nicholas Carter, 105 East Jefferson Blvd., South Bend, Ind., Secretary.
Oklahoma State Medical Association, Oklahoma City, May 11-12. Dr. Lewis J. Moorman, 210 Plaza Court Bldg., Oklahoma City, Secretary.
Texas, State Medical Association of, Fort Worth, May 3-6. Dr. Holman Taylor, 1404 West El Paso St., Fort Worth, Secretary.
West Virginia Medical Association, Charleston, May 17-18. Mr. Charles Lively, 1031 Quarrier St., Charleston, Executive Secretary.

CENTRAL SOCIETY FOR CLINICAL RESEARCH

Fifteenth Annual Meeting, held in Chicago, Nov. 6 and 7, 1942

The President, DR. ARLIE R. BARNES, Mayo Clinic, Rochester, Minn., Presiding

Calcium, Phosphorus and Vitamin D Therapy in Hyperthyroidism

DR. ITALO D. PUPPEL, DR. HAROLD T. GROSS, EMMA K. MCKORMICK, M.Sc., and DR. GEORGE M. CURTIS, Columbus, Ohio: The calcium balance of 3 normal persons, 7 persons with exophthalmic goiter and 4 with toxic nodular goiter was determined under variations of calcium, phosphorus and vitamin D feeding over a total period of about five hundred days.

The disturbances of calcium metabolism in hyperthyroidism usually consisted principally of an increased excretion of calcium through both the gastrointestinal and the urinary system. The blood calcium and phosphorus usually remained within normal limits. These abnormal findings differ greatly from those in hyperparathyroidism, in which the increased excretion occurs almost quantitatively through the urine while both the blood

calcium and phosphorus levels are usually disturbed. They lead to definite differences in the clinical manifestations of the disturbed calcium metabolism in these two disease entities. In hyperparathyroidism with its usual hypercalcemia and hypophosphatemia, metastatic calcification frequently results. Urinary stones occur in about half the cases and constitute one of the most dreaded complications of this disease. In hyperthyroidism, with its usual eucalcemia and euphosphatemia even in the presence of increased calcium excretion equal to or often greater than in hyperparathyroidism, metastatic calcification is rarely observed. Urinary stones occur rarely and are probably only coincidental.

The real danger in feeding high calcium and phosphorus preoperatively in hyperparathyroidism is this increased predisposition to metastatic calcification. In hyperthyroidism there is no such danger, and we have therefore given many of our patients with hyperthyroidism a high calcium, phosphorus and vitamin D diet preoperatively for several years. Not one of these patients has developed the so-called thyroid crisis.

The disturbance of calcium metabolism in hyperthyroidism varies greatly. It is usually temporary, preventable and reversible. It can easily be controlled by ingestion or parenteral administration of extra amounts of calcium supplied in various forms such as calcium in milk, calcium gluconate, calcium lactate with a preparation of crystalline vitamin D_2 and dicalcium phosphate with viosterol by mouth, as well as by calcium chloride intravenously. The disturbance is usually temporary in its effect on bones, but at times and particularly in long standing hyperthyroidism in the presence of insufficient calcium intake permanent bone changes may occur which are not ameliorable to therapy of any type. Practically, this far advanced stage can be treated best by prevention with extra calcium feeding, combined with early diagnosis and treatment of the hyperthyroidism.

Administration of extra calcium, phosphorus and vitamin D is of particular value in hyperthyroid patients who refuse operation, in inoperable cases, in patients who are being treated medically or by x-ray therapy, as well as during the preoperative and postoperative management of the usual hyperthyroid patient until the basal metabolic rate returns to normal.

DISCUSSION

DR. CECIL STRIKER, Cincinnati: Were there any x-ray studies of bone showing deposition of calcium following treatment?

DR. HENRY T. RICKETTS, Chicago: How low were the low calcium diets and what happened to the hyperthyroidism on a diet of normal calcium content?

DR. JOHN TUCKER, Cleveland: Was calcium administered to the hyperthyroid patients without giving the usual preoperative doses of iodine? If this was done, did the calcium have any beneficial effects on the symptoms prior to operation?

DR. R. D. TAYLOR, Indianapolis: What was the effect of the administration of iodine on the calcium metabolism in hyperthyroidism? Does calcium metabolism directly parallel the basal metabolic rate?

DR. ITALO D. PUPPEL, Columbus, Ohio: Several patients had had hyperthyroidism for several years prior to thyroidectomy and calcium therapy and had moderately severe osteoporosis. The evidences by x-ray examination of recalcification after five months of adequate calcium therapy were often not convincing but were present occasionally. It is possible that the degree of calcium loss prior to thyroidectomy was so great that a longer period of time will be required to replace the loss. The relatively low calcium diet which we gave the hyperthyroid patients averaged 520 mg. of calcium daily. Our normal controls remained in equilibrium with this amount of calcium. The hyperthyroid patients, however, showed severe loss of calcium. One exophthalmic goiter patient was provided 800 mg. of calcium daily, an amount which easily kept normal controls in positive calcium balance. This patient also showed a loss of calcium with a negative balance of 330 mg. of calcium daily. Our high calcium diets for the hyperthyroid patients ranged from 1,800 to 3,160 mg. of calcium daily. These diets permitted them to retain calcium. Calcium therapy does improve the musculoskeletal symptoms. With bed rest, high caloric and high calcium intake we usually obtained definite improvement in the general symptomatology and a decrease in the basal metabolic rate of hyperthyroidism. However, when iodine was then supplemented, usually there was further amelioration of symptoms and further decrease of the basal metabolic rate. Calcium does have a definite place as replacement therapy in hyperthyroidism. On the other hand, we do not advocate its use in place of iodine. If iodine administration returns the basal metabolic rate of hyperthyroidism to normal, a decrease in the calcium excretion usually occurs. Increased iodine feeding to 1 patient with severe exophthalmic goiter produced no appreciable change in the basal metabolic rate. The loss of calcium by this patient remained as high as previous to iodine medication.

Classification and Treatment of Male Gonadal Failure

DRS. CARL G. HELLER, RICHARD M. JOHNSON and GORDON B. MYERS, Detroit: Fifty-one men with sexual impotence and other features of gonadal failure were classified into eight different clinical syndromes on the basis of skeletal development, secondary sex characteristics, urine gonadotropic titer and symptomatology. The series included 16 eunuchoids. They were about equally divided between primary pituitary gonadotropic failure and primary testicular failure. Thus, 8 excreted amounts of gonadotropic hormone far below normal levels and 8 excreted amounts above normal levels and equal to castrate excretion. Similarly, some instances of adult gonadal failure were associated with low gonadotropic excretion levels and others with castrate (high) excretion levels.

The gonadotropic titer proved to be a reliable therapeutic index. Each patient with pituitary gonadotropic failure responded well to chorionic gonadotropic therapy. No case with initially high pituitary gonadotropic output responded to administered gonadotropins. Both types responded to substitution therapy with testosterone propionate. Since the gonads are still capable of responding at any age (from 15 to 52 years) it is suggested that in lieu of hormone assays a therapeutic trial of chorionic gonadotropins be given all patients with gonadal failure before substitution therapy is resorted to.

Gonadal failure resulted in the androgen withdrawal symptoms of the male climacteric in 18 of 24 adult cases. Sixteen had elevated gonadotropic titers and 2 had diminished titers. Chorionic gonadotropins alleviated climacteric symptoms in the 2 cases due to pituitary failure. Testosterone propionate was effective in 14 of the 16 cases of primary testicular failure. From comparisons with normal men it was concluded that the male climacteric does not occur physiologically and is a definite disease entity.

DISCUSSION

DR. M. A. BLANKENHORN, Cincinnati: What are your criteria for satisfactory treatment in the hypogonadal eunuchoid type?

DR. W. E. BROWN, Omaha: Chorionic gonadotropins in women cause general gonadal atrophy. How was success measured with gonadotropins in men? Also is the therapy not associated with subsequent atrophy such as found in women?

DR. DANIEL L. SEXTON, St. Louis: What criteria do you have for a good result in those adults that are given chorionic gonadotropins?

DR. CARL G. HELLER, Detroit: There are two treatments for patients with hypogonadism: stimulatory and substitutional. If endocrine studies are not available, the rational approach is to try stimulation first (with gonadotropic hormone). This therapy might produce puberal changes which are maintained. We have had a patient go four months without treatment and maintain sexual potency and secondary sex characteristics. Large doses, 1,500 units of pregnancy urine extract, are used for six weeks. If the gonadotropic hormone treatment fails then substitution therapy with testosterone propionate is begun. The criteria of success consist in increase in size of the penis, increase in sperm count, increase in body hair and a change in the pitch of the voice. The high pitched voice is a definite and serious handicap; it is the reason the patient is discriminated against. We have had difficulty growing beards. It seems that the growth of beard hair occurs slowly, if at all, with any form of therapy. We have taken testicular biopsies after treatment with chorionic gonadotropins and found evidence of stimulation of the testes.

(To be continued)

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1932 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Clinical Pathology, Baltimore

12:597-642 (Dec.) 1942

Monilia Osteomyelitis: Report of Case Resulting from Thrush. J. S. Weingart, D. C. Wirtz and N. W. Irving, Des Moines, Iowa.—p. 597.
Auricular Scabies (Psoroptic Otacariasis) of Rabbit. W. Kaufmann, New York.—p. 601.
Relation of Allergy to Immunity in Experimental Tuberculosis. E. F. Geever, Denver.—p. 606.
Effect of Urine Extracts on Prevention and Healing of Experimental Ulcers in Dogs. D. C. Beaver, D. J. Sandweiss, H. C. Saltzstein, A. A. Farbman and A. W. Sanders, Detroit.—p. 617.
Intracellular Inclusion Bodies in Carcinoma of Adrenal Gland: Case of Multiple Primary Tumors. R. J. Stein, Newport, Vt.—p. 630.

American J. Digestive Diseases, Fort Wayne, Ind.

10:1-44 (Jan.) 1943

*Present Status of Serum Lipase Test. T. A. Johnson and H. L. Bockus, Philadelphia.—p. 1.
External Pancreatic Fistula: Report of Case with Physiologic Observations. M. W. Comfort, A. E. Osterberg and J. T. Priestley, Rochester, Minn.—p. 7.
External Secretion of Pancreas and Diabetes Mellitus. H. M. Pollard, Lila Miller and W. A. Brewer, Ann Arbor, Mich.—p. 20.
*Gastric Mucosa, "Gastritis" and Ulcer. S. Wolf and H. G. Wolff, New York.—p. 23.
Peptic Ulcer in the Aged: Clinical and Postmortem Study. J. Meyer and O. Saphir, Chicago.—p. 28.
Unusual Vascular Diseases Within Abdomen. S. Kimball, M. H. Lipsitz and K. Terplan, Buffalo.—p. 30.

Present Status of Serum Lipase Test.—Further confirmation of the specificity of the serum lipase test is presented by Johnson and Bockus, who from some twelve hundred determinations utilize for their discussion 21 cases of acute pancreatitis, 1 of chronic pancreatitis and 30 of pancreatic cancer. The serum lipase value was above 1 cc. at least once during the course of the illness in 17 (81 per cent) of the 21 cases of acute pancreatitis and in 16 (53.3 per cent) of the 30 with cancer of the pancreas. Analysis suggests that the decrease in serum lipase concentration, following an initial elevated serum lipase, may be due to the subsiding of an inflammatory process or to complete destruction of the pancreas. The serum lipase curve in the 1 case of chronic pancreatitis was indistinguishable from that in cancer of the pancreas. The serum lipase curves in pancreatic cancer suggest that its initial elevation is due to an obstruction to the free flow of pancreatic juice. The subsequent decrease is due either to replacement of pancreatic tissue by the malignant process or to impaired pancreatic function secondary to prolonged pancreatic duct obstruction.

Gastric Mucosa, "Gastritis" and Ulcer.—Wolf and Wolff describe the changes to various stimuli of the gastric mucosa of a 57 year old subject with a permanent gastric fistula, 3.5 cm. in diameter, surgically produced in 1895 because of benign stricture of the esophagus. The congested mucosa was especially susceptible to injury; this suggests that vascular engorgement might predispose to the development and persistence of erosions and changes secondary to inflammation. Sustained hyperemia of the gastric mucosa was accompanied by symptoms of abdominal discomfort and pain. However, after a fast of twelve or more hours, that is, resting gastric mucosa, if the mucosa was struck a sharp blow with the side of a glass rod the area struck became blanched and depressed within one second. It remained so for one to five seconds, depending on the force of the blow. Following this, a slight transitory hyperemia occurred in the same region, which lasted for three to ten seconds. Strong irritants and corrosive agents failed to cause more than a slight to moderate erythema in the gastric mucosa, while they caused a decided reaction with destruction of tissue when applied in similar concentration to the skin. This indicates that the cells lining the stomach are endowed with some special protection against chemical injury. Presumably the special protection is afforded by the thick layer of tenacious mucus adherent to the lining of the stomach and is elaborated in increasing amounts in response to physical and chemical stimuli. To test this protective power, a part of the gastric mucosa was deprived of this covering and then the area was subjected to 1.0 normal hydrochloric acid. Within two minutes a thick layer of grayish opaque mucus appeared over the area exposed to the acid. The application of the drops of acid was increased from twelve to twenty a minute, while the accumulated mucus was sucked away through a pipet. Within five minutes the mucosa beneath became moderately reddened and edematous. Then a mustard suspension was applied, and within five minutes the redness and edema was further accentuated and minute bleeding points became evident as pinpoint black specks on the mucosa. A sharp blow with a glass rod to the gastric mucosa at this time induced minute bleeding points. Rubbing with the blunt end of a glass rod also caused hemorrhage and these mechanical stimuli applied to such an area caused pain. Two of these small hemorrhagic lesions kept in contact with gastric juice for half an hour caused a sharp acceleration of acid secretion and concomitant hyperemia of the whole gastric mucosa which persisted for half an hour after submersion of the hemorrhagic lesions was discontinued. In this phenomenon may lie an explanation of the persistent hyperacidity regularly present in persons suffering from "gastritis" and peptic ulcer. The fact that the base of an ulcerated lesion constantly bathed in acid gastric juice stimulates acid secretion indicates that afferent impulses subserve this reflex without any resulting sensation. Pain probably would follow an adequate chemical stimulus. A small erosion on the peripheral edge of the mucosa lacking in mucus was exposed to the digestive action of gastric juice for four days, when it exhibited the typical punch-out appearance of a chronic peptic ulcer with well defined edges and a granulating base. Traction or pressure on this lesion caused dull gnawing pain. Throughout the four days the whole mucosa was relatively engorged and the rate of acid secretion was significantly elevated. At the end of the four days the ulcer and surrounding area were covered with a protective petrolatum dressing, and within three days healing was complete.

American Journal of Diseases of Children, Chicago

65:1-194 (Jan.) 1943

Basal Heat Production in Relation to Growth: Longitudinal Study on Normal Infants Six to Twenty Months of Age. Helen R. Benjamin and A. A. Weech, New York.—p. 1.
Diabetic Coma, Acute Pancreatitis and Bacillus Welchi Peritonitis. M. M. Steiner and P. C. Tracy, Chicago.—p. 36.
Studies on Oxyuriasis: XXVIII. Summary and Conclusions. Eloise B. Cram, Bethesda, Md.—p. 46.
Streptococcic Antifibrinolysin in Newborn Infants: True and False Tests. J. A. Lichty Jr., Rochester, N. Y., and G. K. Anderson, Chapel Hill, N. C.—p. 60.
Intractable Hypophosphatemic Rickets with Renal Glycosuria and Acidosis (the Fanconi Syndrome): Report of Case in Which Increased Urinary Organic Acids Were Detected and Identified, with Review of Literature. D. J. McCune, H. H. Mason and H. T. Clarke, New York.—p. 81.

American Journal of Ophthalmology, Cincinnati

26:1-118 (Jan.) 1943

Edward Jackson, Student and Teacher. W. H. Crisp, Denver.—p. 1.
Granuloma Inguinale of Eyelid: Report of Case. A. L. Weiner, I. E. Gaynon and M. S. Osherwitz, Cincinnati.—p. 13.
Practical Importance of Aniseikonia. E. Jackson, Denver.—p. 18.
Ocular Findings in Childhood Endocrinopathies. C. Apple and I. P. Bronstein, Chicago.—p. 21.
Results of Glaucoma Surgery. S. A. Fox, New York.—p. 31.
Epidemic Keratoconjunctivitis. M. L. Berliner, New York.—p. 50.
Varicella and Cornea: Case Report. H. D. Rosenbaum, Fort Leavenworth, Kan.—p. 53.
Prostigmine in Treatment of Glaucoma: Its Effect on Intraocular Pressure. P. Montalván, New York.—p. 57.
Are Welders Subject to Depletion of Visual Purple While at Work? H. S. Kuhn and E. C. Wille Jr., Hammond, Ind.—p. 63.
Contracture in Ocular Muscle Paralysis. R. O'Connor, San Francisco.—p. 69.
Case Report of Congenital Grouped Pigmentation of Retina with Maculocerebral Degeneration. G. T. Schwarz, Cleveland.—p. 72.

Archives of Ophthalmology, Chicago

29:1-170 (Jan.) 1943

*Toxoplasmic Encephalomyelitis: VII. Significance of Ocular Lesions in Diagnosis of Infantile or Congenital Toxoplasmosis. F. L. P. Koch, St. Paul; A. Wolf, D. Cowen and Beryl H. Paige, New York. —p. 1.
Medical Considerations of Some Geriatric Problems. G. M. Piersol, Philadelphia.—p. 26.
*Fibroblastic Overgrowth of Persistent Tunica Vasculosa Lentis in Premature Infants: II. Report of Cases—Clinical Aspects. T. L. Terry, Boston.—p. 36.
*Id.: IV. Etiologic Factors. T. L. Terry, Boston.—p. 54.
Relation of Diet to Lenticular Changes in Larvae of Amblystoma Tigrinum. Esther M. Patch, Haddonfield, N. J.—p. 69.
Fundus Oculi in Hypertensive Vascular Disease. M. Cohen, New York.—p. 85.
Bilateral Thrombosis of Posterior Calcarine Arteries with Sparing of Macular Vision. P. R. McDonald, Philadelphia.—p. 92.
Scleral Disease in Rheumatoid Arthritis: Report of Three Cases, in One of Which Both Eyes Were Studied Post Mortem. J. W. Smoleroff, New York.—p. 98.
Emmetropia. E. S. Munson, New York.—p. 109.
Clinical Significance of Aniseikonia. H. M. Burian, Hanover, N. H. —p. 116.

Toxoplasmic Encephalomyelitis.—Koch and his associates describe the ocular changes in 6 cases of infantile toxoplasmic encephalomyelitis, compare and arrange them in a sequence and point out in what way they may be unique and diagnostic. The essential lesion is a focal toxoplasmic chorioretinitis, bilateral and frequently multiple. Almost invariably the macular region in each eye is involved first, but more peripheral lesions often occur. The remaining portion of the retina and the vasculature are normal. Toxoplasmic chorioretinitis is an important diagnostic feature of infantile toxoplasmic encephalomyelitis and it first suggested the presence of the disease in 4 of the 6 cases presented. Toxoplasmic chorioretinitis must be differentiated ophthalmoscopically from pseudoglioma, intraocular tumors, traumatic birth lesions, hereditary cerebromacular degeneration and congenital developmental defects. The diagnostic intraocular lesions in infants and children are severe and extensive focal chorioretinal lesions, bilateral involvement of the macular region, peripheral involvement of one or more quadrants of the retina and choroid, punched out appearance of large and small lesions in the late phase, massive chorioretinal degeneration, associated congenital ocular defects, rapid development of sequential optic nerve atrophy and usually a constant clarity of the media. The pathologic changes are necrotizing and inflammatory lesions in the retina and in the choroid similar to those found in the brain.

Tunica Vasculosa Lentis in Infants.—Seven instances of a fibroblastic sheath behind the crystalline lens in both eyes of infants born about eight weeks prematurely are reported by Terry. The syndrome, which is usually bilateral, is composed of widespread primary and secondary manifestations related to persistence of the hyaloid artery and tunica vasculosa lentis, growth of embryonic connective tissue behind the lens and persistence of fetal fibrillar vitreous. It is usually observed four to six months after birth. The condition must be differentiated from retinoblastoma and congenital cataract. Glaucoma is an important complication. Treatment has been temporization, irradiation and closure of the hyaloid artery by diathermy. Complete excision of the membrane seems unwise, as pathologic specimens show that ciliary processes and retina adhere to the fibroplastic membrane. Intraocular hemorrhage and inflammation were found in the embryonic connective tissue of some pathologic specimens. A search for the essential etiologic factor or factors discloses that prematurity, often with twinning, is an important predisposing, but not invariably an essential, factor. The degree of prematurity appears to influence the nature of the involvement. The outstanding theoretical cause is a precocious increase in blood pressure brought on before the hyaloid artery and the tunica vasculosa lentis disappear, initiated by such normal factors as adaptation to extrauterine life or such abnormal factors as patent ductus arteriosus, dehydration or use of drugs. After the development of increased blood pressure, hypertrophy of the hyaloid arterial system takes place, causing the fibrillar vitreous and the growth of supporting embryonic connective tissue to persist.

Canadian Medical Association Journal, Montreal

48:1-92 (Jan.) 1943

Restoration of Functional Capacity of Stomach When Deprived of Its Main Arterial Blood Supply. B. P. Babkin, J. C. Armour and D. R. Webster, Montreal.—p. 1.
Work of the Medical Branch of the Royal Canadian Navy. A. McCallum, Ottawa, Ont.—p. 11.
*Plastic Film Treatment of Experimental Burns. H. G. Skinner and R. A. Waud, London, Ont.—p. 13.
Royal Canadian Navy Color Vision Test Lantern. D. Y. Solandt and C. H. Best, Toronto.—p. 18.
Complication of Mumps—Swelling Over the Manubrium Sterni. C. S. Barker, St. Thomas, Ont.—p. 22.
Death Following Sulfathiazole Therapy. M. A. Simon and M. Kaufmann, Montreal.—p. 23.
Bronchomoniliasis. W. A. Farrell, Fort William, Ont.—p. 28.
Note on Rose Hips and Evergreens as Sources of Vitamin C. G. Hunter and J. Tuba, Edmonton, Alta.—p. 30.
Use of Evaporated Half Skimmed Milk in Infant Feeding. C. E. Snelling, Toronto.—p. 32.
Method of Treating Psoriasis. P. A. O'Leary, Rochester, Minn. —p. 34.
Obscure Pains in Chest, Back or Limbs. F. G. Allison, Winnipeg, Man. —p. 36.
Effective Use of Vitamins. C. W. Scull, Abington, Pa.—p. 39.
Prevention of Bullous Impetigo in Hospital Nurseries. R. P. Kinsman, Vancouver, B. C.—p. 44.
Strangulated Hernia with Gangrenous Bowel Treated by Multistage Operation. A. W. S. Hay, Petawawa, Ont.—p. 46.
Maternity Statistics. F. S. Hobbs, Vancouver, B. C.—p. 48.
Tuberculin Testing of Young Adults, with Particular Reference to Vollmer Patch Test. F. G. Pedley, Montreal.—p. 52.

Plastic Film Treatment of Experimental Burns.—Skinner and Waud compare the healing power, anti-infective ability and other properties of five agents on the healing of experimentally produced wounds in rabbits. Data show that burns treated with two sulfonamide-triethanolamine burn fluids which result in a film when dry healed at least five days before those treated with tannic acid, ten days before those treated with weak triple dye solution and forty days before those treated with strong triple dye solution. The anti-infective ability of strong triple dye solution is upheld, but this fact does not overcome its adverse effect on healing time. Of the burn fluids, the one that contained phemerol appeared to be of more value against infection. Weak triple dye or tannic acid was not as effective against infection as the other burn fluid. The burn fluids were more easily applied and gave a most satisfactory eschar, which was easy to remove with warm saline solution without damage to the surface of the wound. All the other methods caused damage to granulation and epithelium when the eschar was removed.

Illinois Medical Journal, Chicago

83:1-76 (Jan.) 1943

Treatment of Soft Tissue Injuries. F. W. Slobe, Chicago.—p. 21.
Management of Burns. B. B. Reeve, Chicago.—p. 26.
Minimal Fracture Requirements. J. J. Callahan, Chicago.—p. 31.
Preventive Therapy in Recurrent Urinary Lithiasis. E. H. Droegemueller, Elmhurst.—p. 34.
Rationale in Treatment of Infants and Children. A. J. Fletcher, Danville.—p. 38.
Virus Pneumonia. H. N. Kamin, Chicago.—p. 41.
Theory of the Origin of Cancer: Preliminary Report. A. L. Magnelia, J. H. Kaplan and E. Hyson, Rockford.—p. 43.
Considerations Regarding Depth of Anesthesia. W. H. Cassels, Chicago. —p. 46.
Myth of Postoperative Pneumonia. J. R. Buchbinder, Chicago.—p. 50.

Journal of Nervous and Mental Disease, New York

97:1-132 (Jan.) 1943

Didactic Note on Alcoholism. M. Moore, Boston.—p. 1.
Myasthenia Gravis Including Case Report and Neurologic Autopsy. H. G. Hadley, Washington, D. C.—p. 6.
Neurologic Effects of Syphilis. S. H. Epstein, Boston.—p. 11.
Rorschach Examinations in Acute Psychiatric Admissions. K. S. Hitch, Camp Joseph T. Robinson, Ark.—p. 27.
Treatment of Psychotic Patients in General Hospitals and Sanitariums (Statistics and Implications). J. Weinberg and H. H. Goldstein, Chicago.—p. 40.
Analysis of Disturbances of Higher Cortical Functions, Agnosia, Apraxia and Aphasia. H. A. Teitelbaum, Baltimore.—p. 44.
Comparative Study of Combined Metrazol Hypoglycemic Shock Treatment and Spontaneous Improvements in Schizophrenia. J. Notkin, L. E. Watts, G. W. Shannon, C. E. Niles and F. J. DeNatale, Poughkeepsie, N. Y.—p. 62.

New Orleans Medical and Surgical Journal

95:305-356 (Jan.) 1943

Future of Patient with Coronary Occlusion. C. A. Stone, Galveston, Texas.—p. 305.
Rational Management of Bronchiectasis. C. R. Gowen, Shreveport, La. —p. 311.
War Wounds of Chest. H. W. Harrison, Shreveport, La.—p. 315.
*Surgical Treatment of Pelvic Thrombophlebitis: Ligation of Inferior Vena Cava and Ovarian Veins: Preliminary Report. C. G. Collins, J. R. Jones and E. W. Nelson, New Orleans.—p. 324.
*Use of Darkfield Microscope for Diagnosis of Generalized Secondary Lesions of Syphilis. O. F. Agee, New Orleans.—p. 329.
Mumps: Relationship Between Submaxillary Gland Involvement and Incidence of Orchitis. A. Oppenheim, Arcadia, La., and H. H. Golz, Fort Oglethorpe, Ga.—p. 332.
*Meningitis Caused by the Higher Fungi. J. E. Skogland, New Orleans. —p. 334.
Cruveilhier-Baumgarten Syndrome. F. E. Bruno, New Orleans.—p. 339.

Surgical Treatment of Pelvic Thrombophlebitis.—Collins and his co-workers present 3 cases of pelvic thrombophlebitis treated by ligation of the ovarian veins and the inferior vena cava. One case was postpartal, 1 followed an attempted criminal abortion and 1 followed a vaginal hysterectomy. The 3 patients have fully recovered and do not show any ill effects from the ligation. However, the venous pressure in the lower extremities of the 3 is elevated, but there is no edema. The venous pressure has decreased in all as the interval from the date of the operation increases. This suggests that in the near future the venous pressure may return to or vary little from the normal. Following vena cava ligation, bilateral lumbar sympathetic block should be carried out to enhance the development of collaterals and to relieve any postoperative edema. If a patient feels faint and anxious while the block is being administered, the procedure should be discontinued immediately and attempted again in forty-eight hours. Roentgen examination of the chest is imperative in all cases, as emboli and infarction may be present without clinical symptoms.

Secondary Lesions of Syphilis.—The use of the darkfield microscope on secondary dry or closed cutaneous syphilitic lesions can expedite treatment by obtaining a positive darkfield report instead of waiting for a positive serologic test. Agee reports 10 cases; 8 were seen in the New Orleans Health Department Clinic and 2 in the Tulane Clinic at Charity Hospital. For the test, the surface of the lesion must be abraded vigorously with a scalpel or dry gauze. If serum does not exude freely the area is squeezed to express sufficient material. The treponemes do not seem quite as active as those from open lesions, perhaps because of the pressure exerted.

Meningitis Caused by the Higher Fungi.—The four higher fungi causing meningitis that Skogland discusses are Actinomyces, Blastomyces, torula and coccidioides. Man apparently acquires actinomycotic meningitis from contact with infected hay or grain. Infection almost always occurs following a primary infection elsewhere in the body which spreads to the meninges by direct extension. The symptomatology of actinomycosis of the central nervous system depends on the several forms (meningitis, cerebral abscess and cerebellar abscess) that the pathologic reaction may take. The prognosis is poor; all cases terminate fatally. Therapy is entirely symptomatic, although empirically iodides may be prescribed. Infection with Blastomyces (Oidiomyces) is cutaneous, with primary involvement usually on the face or hands, and in a systemic form in which widespread dissemination of the organism occurs following invasion through the respiratory tract. The pathologic changes in the central nervous system are usually nonspecific and closely resemble those associated with tuberculous meningitis. It is characterized by the usual symptomatic course lasting several months. There is no satisfactory therapy, and it is doubtful that roentgen therapy, excision and iodides have any beneficial effect after the meninges have been invaded. Torula meningitis is most common in male adults. The respiratory tract is the usual port of entry. Dissemination then takes place through the blood stream or lymph nodes when the central nervous system of at least half the cases is involved; other organs also are involved. The pathologic changes in the central nervous system are variable and the symptomatology varies with their nature and extent. There is no specific treatment, but symptomatic measures may produce temporary relief. Coccidioidal granuloma, an endemic disease, occurs principally in the San Joaquin Valley, California. The fungus gains entrance through the lungs or the skin and subsequently is carried by the blood stream to other organs. In approximately 25 per cent of patients the meninges are involved. The disease occurs usually in adults and is more common in men. The pathologic changes vary with the duration of meningeal involvement. The symptoms are nonspecific but are similar to those of other chronic meningitides, often with superimposed evidence of internal hydrocephalus. Coccidioidal meningitis always terminates fatally. Symptomatic therapy is the same as for other forms of meningitis. When localized spinal compression exists, laminectomy, in an attempt to remove granulomatous tissue, may be justified.

North Carolina Medical Journal, Winston-Salem

4:1-40 (Jan.) 1943

The Bookish Theoric. J. L. Ward, Asheville.—p. 1.
Chemical Warfare in Civilian Defense. G. T. Harrell, Winston-Salem. —p. 4.
Tetanus and Essentials of Its Successful Treatment. V. S. Caviness, Raleigh.—p. 6.
Stimulating Influence of Sodium Citrate on Cellular Repair in Kidney Injured by Uranium Nitrate. G. L. Donnelley and R. L. Holman, Chapel Hill.—p. 11.
Diagnosis and Treatment of Thyroid Diseases. P. McBee, Marion. —p. 12.
Medical and Health Evolution in Durham, N. C. W. C. Davison, Durham.—p. 14.
Glance at Ancient Medicine. A. C. Mitchell, Chapel Hill.—p. 17.

Ohio State Medical Journal, Columbus

39:1-96 (Jan.) 1943

Auricular Fibrillation. C. F. Garvin, Cleveland.—p. 18.
Treatment of Arterial Hypertension with Potassium Thiocyanate. H. Kotte, Cincinnati.—p. 20.
Osteoarthritis of Hip, with Observations on Certain Features Which It Has in Common with Charcot's Disease. L. C. Kelly, New York. —p. 26.
Report of Four Outbreaks of Epidemic Diarrhea of the Newborn in Ohio. Susan P. Souther, Columbus.—p. 30.
Ocular Manifestations of Syphilis. C. J. Streicher, Canton.—p. 32.
Penile Cancer: Report of Case in a Luetic; Review of Literature; Discussion and Treatment. V. C. Laughlin, Cleveland.—p. 35.
Contact Dermatitis. H. L. Claassen, Cincinnati.—p. 40.
Treatment of Herpes Zoster. B. F. Barney, Columbus.—p. 42.
Anesthetics in Appendicitis, from the Cleveland Appendicitis Survey: II. R. M. Watkins, Cleveland.—p. 43.
Current Thought in Life Insurance. D. E. Yochem, Columbus.—p. 44.
Importance of Copper in Nutrition. J. Forman, Columbus.—p. 48.
Carcinoma of Suprapapillary Portion of Duodenum. T. C. Laipply, Cleveland.—p. 50.

Psychiatric Quarterly, Utica, N. Y.

17:1-224 (Jan.) 1943

Psychoanalysis of Psychoses: I. Errors and How to Avoid Them. P. Federn, New York.—p. 3.
Preliminary Curarization in Electric Convulsive Shock Therapy. P. T. Cash and C. S. Hoekstra.—p. 20.
Dissociated Personality: Case Report. S. Lipton, Cincinnati.—p. 35.
Diagnosis of Psychogenic Factors in Disease by Means of Rorschach Method. M. R. Harrower-Erickson, Madison, Wis.—p. 57.
Abnormal Brachial Blood Pressure Response to Postural Change in Patients Suffering from Psychoses of the Senium: Control by Thyroid. D. E. Cameron, D. Mele, H. S. Hirst and F. Feldman, Albany, N. Y.—p. 67.
Note on Pneumoencephalogram and Electroencephalogram Findings in Chronic Mental Patients. E. V. Semrad; and K. H. Finley, Boston. —p. 76.
Rorschach Diagnosis of Cerebral Arteriosclerosis. K. S. Hitch, Fort Dix, N. J.—p. 81.
Psychology of Dementia Precox. P. Milici, Kings Park, N. Y.—p. 87.
Convulsions Following Abrupt Withdrawal of Barbiturate: Clinical and Electroencephalographic Studies. S. R. Brownstein and B. L. Pacella, New York.—p. 112.
Interpretation of Antisemitism. G. M. Davidson, Ward's Island, N. Y. —p. 123.
Schizophrenia in Cryptogenic Narcolepsy: Report of Case. S. R. Lehrman, Toledo, Ohio, and E. J. Weiss, Washington, D. C.—p. 135.
Results with Electric Convulsive Therapy in 200 Cases of Schizophrenia. L. B. Kalinowsky and H. J. Worthing, West Brentwood, N. Y. —p. 144.
Outcome of Electric Shock Therapy in New York Civil State Hospitals. B. Malzberg, Albany, N. Y.—p. 154.
Evaluation of Factor of Depression of Brain Metabolism in Treatment of Schizophrenia. C. H. Bellinger, C. F. Terrence, Brooklyn; B. Lipetz and H. E. Himwich, Albany, N. Y.—p. 164.

Public Health Reports, Washington, D. C.

58:33-68 (Jan. 8) 1943

Distribution of Health Services in Structure of State Government: Chapter VIII—Industrial Health Activities by State Agencies. J. W. Mountin and Evelyn Flook.—p. 33.

58:69-120 (Jan. 15) 1943

Public Health Service Drinking Water Standards. Report of Advisory Committee on Official Water Standards.—p. 69.
Manual of Recommended Water Sanitation Practice.—p. 83.

South Carolina Medical Assn. Journal, Florence

39:1-28 (Jan.) 1943

Story of Appendicitis. R. Fitz, Boston.—p. 1.
Bilateral Castration for Carcinoma of Prostate. J. E. Boone, Columbia. —p. 5.
Sulfadiazine in Treatment of Pneumococcic Meningitis. G. D. Johnson, Spartanburg.—p. 7.

Surgery, St. Louis

12:841-1000 (Dec.) 1942

*Ligation of Patent Ductus Arteriosus: Report of Results in Seven Cases. G. H. Humphreys, New York.—p. 841.
Experimental Study of Shock, with Special Reference to Its Effect on Capillary Bed. G. T. Root and F. C. Mann, Rochester, Minn.—p. 861.
*Effects of Concentrated Serum in Contrast to Iso-Osmotic Plasma on Normal and Dehydrated Dogs in Shock. S. O. Levinson, R. E. Weston, Martha Janota and H. Necheles, Chicago.—p. 878.
*Surgical Excision of Primary Tumor (Hamartoma) in Infant Seven Months Old with Recovery. C. D. Benson and G. C. Penberthy, Detroit.—p. 881
Gastric Secretory Depressant in Gastric Juice. A. Brunschwig, R. A. Rasmussen, E. J. Camp and R. Moe, Chicago.—p. 887.
Halsted Radical Mastectomy: Five Year Results in 246 Consecutive Operations at the Same Clinic. B. F. Hoopes and A. B. McGraw, Detroit.—p. 892.
*Peritoneal Response to Locally Implanted Crystalline Sulfonamide Compounds. T. D. Throckmorton, Rochester, Minn.—p. 906.
Comparative Blood Concentrations of Sulfaguanidine, Sulfanilamide and Sulfathiazole After Administration Orally, Peritoneally and Pleurally to Dogs. A. M. Ambrose, Louisville, Ky., and H. B. Haag, Richmond, Va.—p. 919.
Drainage of Exteriorized Liver (External Hepatostomy): Palliative for Jaundice. W. W. Babcock, Philadelphia.—p. 925.
Surgical Approach to Lesions of Upper Sciatic Nerve and Posterior Aspect of Hip Joint. H. C. Naffziger, San Francisco, and N. C. Norcross, Mare Island, Calif.—p. 929.
Postoperative ("Anesthetic") Paralysis of Brachial Plexus: Review of Literature and Report of Nine Cases. E. G. Clausen, Oakland, Calif.—p. 933.
Platybasia: Report of Case Treated Surgically with Improvement. R. H. Stevens, Boston.—p. 943.
Preservation of Transversalis Muscle in Gas Gangrene of Trunk. C. Lyons, Boston.—p. 952.
Extensive, Mutilating Facial Defect; Cosmetic Correction with Latex Mask. A. M. Brown, Chicago.—p. 957.

Ligation of Patent Ductus Arteriosus.—Humphreys obliterated surgically a patent ductus arteriosus eight times in 7 children between 9 and 13 years of age. Roentgen, electrocardiographic and electrostethographic studies aided in proving the diagnosis. In several children one or more of the usual diagnostic criteria were absent, yet a patent ductus was always found. A low diastolic pressure was the most consistent observation. Associated skeletal anomalies were present in 3 and a congenital squint and torticollis in 1. Six ligations were carried out because of systemic effects of the mechanical circulatory abnormality and two to overcome subacute bacterial blood stream infection which had resisted adequate sulfonamide therapy. There were no postoperative deaths. The operation overcame the mechanical circulatory symptoms of 4 patients and the improvement has been maintained for twenty-eight, twenty-two, twenty and seventeen months, respectively. In 1 the patency recurred, apparently the result of cutting through the ligature; this was subsequently ligated successfully. In 1 the result is uncertain. In the 2 in whom infection was present at the time of operation, subsequent blood cultures have not shown organisms and the patients are conspicuously improved six and seven months after operation. In the year that has elapsed since the article was written, all but 1 of the patients continue in good health; the 1 in whom the result was uncertain died of complications arising from a postoperative aneurysm of the ductus. Nine additional patients have since been operated on without operative mortality. Five, operated on because of systemic symptoms, have shown moderate to pronounced benefits. Four were operated on because of subacute blood stream infection; 1 has been free of infection for nine months; 1 died two months after operation of bacterial endocarditis due to an associated interventricular septal defect, 1 is living six months after operation with persistent murmur and subacute blood stream infection and 1 is in the postoperative period.

Serum and Plasma in Shock.—On the basis of their experience with shock in dogs produced by graded hemorrhage, Levinson and his associates feel that concentrated blood protein solutions must be used circumspectly, especially in dehydrated individuals. Concentrated plasma or serum was less effective in alleviating shock and in maintaining life thereafter than was normal plasma or serum. The state of hydration was an extremely important factor in the ability of an animal to withstand shock and its response to therapy. A more profound state of shock developed in dehydrated animals. Their response to plasma or serum infusion, and particularly to concentrated solutions, was decidedly poorer than that of normal animals. Therefore when concentrated plasma or serum is administered, particularly to dehydrated individuals, the degree and duration of improvement are apt to be incomplete and transient. If only concentrated serum or plasma is available, additional normal plasma or saline solution should be administered at the earliest possible moment. The amount of citrate contained in plasma may be sufficient to produce tetany if large amounts are administered rapidly.

Surgical Excision of Hamartoma in Infant.—Benson and Penberthy report the successful and complete excision of a primary encapsulated tumor (hamartoma) of the liver in an infant of 7 months. Three months after discharge the infant was in excellent health. All such infants deserve exploratory laparotomy because, in spite of the fact that hepatic tumors in them carry a poor prognosis, occasionally a benign tumor will be found. Hamartoma of the liver can be considered benign because it is well encapsulated, it has embryonal characteristics, it does not tend to invade neighboring tissue, no mitotic figures are found microscopically, metastasis does not occur and symptoms are due to the progressive displacement of neighboring structures by the tumor.

Peritoneal Response to Sulfonamides.—Throckmorton studied the peritoneal response of albino rats to crystalline sulfonamide compounds, with special regard to the drugs' possible effects on the local peritoneal defense mechanism. The animals withstood laparotomy very well. Peritoneal fluid was obtained in all instances by puncture. The drugs, 1 Gm. per kilogram of weight implanted intraperitoneally at laparotomy, were sulfanilamide, sulfathiazole, sulfapyridine, sulfadiazine, sulfamethyldiazine and sulfanilylguanidine. Each of them produced some peritoneal reaction: cellular changes in the peritoneal fluid. These reactions are nonspecific and depend on a foreign body reaction of the tissues to the drug and on the innate irritant properties of some of the compounds. The response produced by the rapidly dissolving and inert sulfanilamide is meager, but that initiated by sulfapyridine is so violent that masses of drug are walled off from the general peritoneal cavity. Between these two responses is the cellular response of sulfathiazole, which is the equal of peritoneal vaccination. The ability of sulfathiazole to enhance the local cytologic defense mechanism, and the prolonged bacteriostatic property of sulfonamides, would seem to make it the sulfonamide compound of choice for intraperitoneal use. The actual killing and disposal of the attenuated bacteria are performed by the local cellular defense mechanism. The vigorous response of sulfapyridine causes it to be walled off from the general peritoneal cavity so rapidly as to reduce even its effectiveness as a bacteriostatic agent.

War Medicine, Chicago

3:1-112 (Jan.) 1943

Nutrition in Aviation Medicine. H. R. Bierman.—p. 1.
Neuropsychiatric Program for a Replacement Training Center. L. E. Stilwell and J. Schreiber.—p. 20.
Effects of Centrifugal Acceleration on Living Organisms. G. C. Ham, Charlottesville, Va.—p. 30.
Cryptic Nostalgia. C. L. Wittson, H. I. Harris and W. A. Hunt. —p. 57.
d-Desoxyephedrine: Review. A. C. Ivy and F. R. Goetzl, Chicago. —p. 60.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Journal of Hygiene, London

42:451-570 (Oct.) 1942

Influence of Social Conditions on Diphtheria, Measles, Tuberculosis and Whooping Cough in Early Childhood in London. G. P. Wright and Helen Payling Wright.—p. 451.
*Staphylococcus Aureus in Milk of Nursing Mothers and Alimentary Canal of Their Infants: Report to the Medical Research Council. J. T. Duncan and Jacqueline Walker.—p. 474.
Some New Observations Bearing on Nature of Pleuropneumonia-like Organism Known as L1 Associated with Streptobacillus Moniliformis. Emmy Klieneberger.—p. 485.
Reclamation of Used Agar. J. Brodie and D. Stiven.—p. 498.
Fluorosis and the Parathyroid Glands. L. Spira.—p. 500.
*Anemia in Women and Children on Wartime Diets. Lucy Wills, Helen M. M. MacKay, Kaitilin Bingham and R. H. Dobbs.—p. 505.
Cultural Characters and Pathogenicity for Some Laboratory Animals of Vole Strain of Acid Fast Bacillus. A. S. Griffith.—p. 527.
Studies in Immunization by a Species Antigen: I. Preparation of Species Antigen from Pneumococci. H. B. Day.—p. 532.
Comparative Studies on Salmonella Strains Isolated in Palestine from Camels and a Human Being. L. Olitzki—p. 547.
Indexes of Physical Development in Children. A. W. Tuxford.—p. 549.
Bacteriologic Classification of Principal Cultures Used in Rat and Mouse Control in Great Britain. P. H. Leslie.—p. 552.

Staphylococcus Aureus in Milk of Nursing Mothers.—Duncan and Walker tried to determine the incidence of Staphylococcus aureus in the intestine and throat of morbid and healthy newborn infants and in the milk of their mothers; from January 1940 to January 1941 more than 2,500 swabs of materials from these sources were examined. During the last eight months, when the work was interrupted by enemy action, 82 mothers and their babies were examined at one hospital; from only 3 of the 82 mothers or babies Staphylococcus aureus was not obtained. At another hospital, situated approximately 26 miles away, the incidence was less but still high. With few exceptions the coccus cultivated from the mother's milk was of the same kind as that from the baby's throat and usually also that from its rectum. In a series of 87 mothers and their babies the coccus was found first in the throats of 33 babies, first in the milk of 15 mothers and simultaneously in the mother and the baby in 39 instances. The presence of Staph. aureus was not associated with any serious disturbance of health, although the types of the organism identified were also found in some inflammatory and suppurative conditions in the women and their babies. The transmission of the staphylococci among the babies and from the baby to the mother may also be effective for the transmission of more virulent or toxigenic staphylococci, with graver consequences.

Anemia in Women and Children on Wartime Diets.—Between September 1941 and January 1942 Wills and her co-workers estimated the hemoglobin of 544 women and 530 children by the Haldane method. The values obtained were compared with those of similar groups investigated before the war. The mean hemoglobin value for the women was 89.5 per cent; the range was from 56 to 120 per cent. The mean is similar to that obtained by Davidson and his associates in 1937 for a group of nulliparous women from the poorest class in Aberdeen. In 1931 the mean figure of 98.3 per cent was obtained by Price-Jones for 100 supposedly healthy nurses and women students, and a mean figure of 100.5 per cent for 116 women was obtained by Jenkins and Don in 1933. The hemoglobin percentage was below 90 in 54 per cent and below 80 in 10 per cent of the present authors' subjects. In Price-Jones's series no hemoglobin value was below 90 per cent, though in Jenkins and Don's series it was below 90 in 9 per cent and below 80 in 1 per cent. The curve of the mean hemoglobin values of 364 children between 6 months and 5 years of age at successive ages approximates the curves of ten years ago for British children not receiving medicinal iron. The average hemoglobin level at 6 to 12 months was 75.4 per cent, between 1 and 2 years 72.8 per cent and thereafter it gradually rose until between 4 and 5 years it reached 81.8 per cent. The lowest levels were among children less than 2 years of age. The hemoglobin level of these children must be considered pathologically low. The incidence of severe anemia was lower in a welfare group of children than in other groups and was highest among children in residential nurseries. The mean hemoglobin level of 90 school children from 5 to 13 years of age was 80.3 per cent (about 10 per cent lower than Davidson's 1935 mean for poor children in Aberdeen), of 38 school children from 13 to 15 it was 89.3 per cent and of 38 adolescent girls working at a factory it was 98.7 per cent. The authors believe that the general lowering of the mean hemoglobin value of older subjects and the low curves obtained for the younger children are the expression of a nutritional anemia and that iron deficiency is one important etiologic factor, but that other factors have also played a part in the production of this anemia. It is probable that among women and school children other dietetic deficiencies are implicated, and that in nurseries a high incidence of infection has increased the incidence and severity of an anemia primarily due to an iron deficiency. The bearing of this anemia on the health of the nation is of sufficient importance to call for immediate official action and further investigation.

Lancet, London

2:745-772 (Dec. 26) 1942

*Tetanus in the Middle East: Effects of Active Immunization. J. S. K. Boyd and J. D. Maclennan.—p. 745.
Long Incubation Period of Syphilis and Elusive Primary Sore. Mary Michael-Shaw.—p. 749.
*Zinc Peroxide, Proflavine and Penicillin in Experimental Clostridium Welchi Infections. J. McIntosh and F. R. Selbie.—p. 750.
Control of Pulmonary Tuberculosis in Mental Hospitals. W. P. Berrington and C. E. Greenwood.—p. 752.
Slit Lamp Microscope in Nutrition Surveys: Observations in School Children. J. H. Kodicek and J. Yudkin.—p. 753.

Active Immunization Against Tetanus.—Boyd and Maclennan record the incidence of tetanus during the first two years of war in the Middle East and assess the part played by active and passive immunization in its prevention. Despite the fact that Clostridium tetani is relatively rare in samples of soil in the Middle East, it is found in wounds. In 214 cultures of wounds received from different hospitals Cl. tetani was found in 18 (8.4 per cent). In another hospital swabs from 494 cases revealed one or more species of clostridium in 66, including 20 terminal spored anaerobes; 2 of these were Cl. tetani. In the period under review, 18 cases of clinical tetanus have been reported and the evidence in favor of active immunization appears to be definite. Of the 18, 5 were in men who had been actively immunized, 4 with two doses and 1 with three doses. However, none of the 5 received the 3,000 prophylactic units of tetanus antitoxin after being wounded. Of these 5, 2 recovered. Of the 13 patients who had not been immunized 1 received a single dose of 1 cc. of tetanus toxoid three and a half months before he was wounded, 3 were Italian prisoners and 1 an Eritrean prisoner regarding whose inoculation history nothing is known. There were six fatalities. It is known that 3 of these 6 received prophylactic tetanus antitoxin. None of the 7 patients who recovered seem to have received any prophylactic tetanus antitoxin. There was a general tendency toward a long incubation period in all the patients. This cannot be attributed to antitoxin treatment but may in some way be related to effective surgical removal of all but the most trivial foci of infection. Evidently the protection afforded by active immunization has its "ceiling." It appears capable of inactivating toxin from a wound from which the bulk of necrotic tissue has been removed, but not from one forming massive quantities of toxin in extensive necrotic areas. The closed plaster technic was not without danger to 1 of the patients: a mass of necrotic tissue was unsuspected until symptoms supervened, when it was too late for benefit to ensue from its removal. The little that is known about tetanus in the British Expeditionary Force in France during 1939-1940 reveals 8 cases among the unprotected 10 per cent and none among the 90 per cent actively immunized.

Zinc Peroxide in Clostridium Welchi Infection.—McIntosh and Selbie found that the local application of zinc peroxide was apparently of no value in preventing the development of experimentally produced Clostridium welchi infection in mice when the organism had invaded the tissues. Proflavine was of greater value than sulfanilamide and was at least as good as sulfathiazole in the local prophylaxis and treatment; therefore its use as a wound dressing should be further explored. Penicillin injected at the site of infection within three hours of infection was a powerful prophylactic and in this respect it was superior to proflavine and the sulfonamides.

Presse Médicale, Paris

50:145-168 (Feb. 11-14) 1942

Problem of Herpetic Meningitis: Clinical and Experimental Studies. M. Janbon, J. Chaptal and M. Labraque-Bordenave.—p. 145.
Case of Glandular Bisexuality in a Boy: Human Pseudohermaphrodism. Costantini and Toreilles.—p. 148.
*Two Simple Procedures of Extemporaneous Sterilization of Drinking Water. H. Violle and R. Seigneurin.—p. 150.
New Roentgenologic Method of Topographic Marking and Localization. P. J. Coletsos and L. H. Coletsos-LaFay.—p. 151.

Sterilization of Drinking Water.—The procedure suggested by Violle and Seigneurin has the advantage of being able to sterilize extremely contaminated water in fifteen minutes and does not require filtration. The authors found that 1 liter of water containing 12 billion of Escherichia coli is sterilized in fifteen minutes by the addition of 1 mg. of potassium permanganate and 1.5 Gm. of citric acid. Typhoid, paratyphoid A and B, dysentery bacilli and cholera vibrios are destroyed by the same dose. The advantage of the method lies in the fact that the amount of permanganate used is only one fiftieth of that utilized in other procedures of water sterilization. Decolorization by hyposulfite is unnecessary, because it takes place spontaneously in about fifteen minutes. Filtration is superfluous, because the quantity of manganese oxide formed is harmless. The water so treated is rather acid (p_H about 4.2). In order to render it more potable it can be neutralized with sodium bicarbonate. The method can be simplified by combining 1.5 Gm. of citric acid and 1 mg. of potassium permanganate in a tablet with 0.5 Gm. of lactose as an excipient. This tablet, when placed in water, produces first a rose color and then a yellowish brown, but at the end of fifteen minutes the water is again transparent. At this time a tablet containing 2 Gm. of sodium bicarbonate and 0.25 Gm. of lactose is added. This effects neutralization of the citric acid and a slight liberation of carbonic gas. The simplicity, efficacy and rapidity make the method valuable for explorers, in floods, epidemics, wars and whenever industrial purification is inadequate or nonexistent. The second procedure has the advantage of requiring only a single tablet which produces its effect in twenty minutes. The composition of this tablet is potassium permanganate 0.001 Gm., citric acid 0.02 Gm., potassium iodide 0.02 Gm., potassium iodate 0.01 Gm. and lactose 0.15 Gm. This form of sterilization (single tablet) can be used whenever, as is usually the case, the water does not contain more than 1 billion of Escherichia coli or of typhoid bacilli.

Bol. del Inst. de Clínica Quirúrgica, Buenos Aires

18:463-606 (Aug.) 1942. **Partial Index**

Diagnosis of Acute Appendicitis. O. Ivanissevich.—p. 467.
Biologic Treatment of Tuberculosis. C. Robertson Lavalle.—p. 472.
*Value of Cystostomy in Treatment of Ruptures of Urethra. R. L. Roccatagliata.—p. 485.
Closure of Anterior Thoracotomies: Technical Detail. M. M. Brea.—p. 533.
Star Shaped Laparotomy of Arce. C. I. Rivas.—p. 535.
Symptomatology of Tumors of Mammary Gland. C. I. Rivas.—p. 540.
*Surgical Treatment of Cancer of Esophagus. R. C. Ferrari.—p. 545.

Cystostomy for Rupture of Urethra.—Roccatagliata analyzes 35 cases of rupture of the urethra. He concludes that: 1. Diagnosis of the existence, localization and severity of a urethral rupture is to be based exclusively on the clinical symptoms and their interpretation. 2. The symptoms determine the treatment to be employed. 3. Early endourethral exploration is not to be practiced. 4. Urinary retention demands an immediate cystostomy. 5. Large hematomas should be incised and drained, following hypogastric evacuation of the urine; however, in case of small hematomas an expectant attitude is justified. 6. Hemorrhage from the urethra does not endanger life and does not require local treatment. Urethral lavage and catheterization have been discarded. 7. Urethral repair by suture should be postponed for at least six weeks. 8. A permanent endourethral tube should never be left in contact with the suture. 9. Endourethral examination should not be done too soon after trauma or suture. It should not be practiced before inflammation of the scar has completely subsided, because the resulting irritation would produce hypertrophy, which would lead to stenosis of the passage. Dilations should not be begun before six weeks have elapsed. 10. In cases in which extensive destruction prevents the approximation of the two ends, their suture to the perineum and a secondary urethral reconstruction, according to Guyon-Legueu, is recommended (perineal urethrostomy). 11. Early hypogastric cystostomy is most important in the surgical treatment of urethral ruptures prevents infection and urinary contamination of the lesion, and contributes much to successful repair. It made possible elimination of the permanent catheter.

Surgical Treatment of Cancer of Esophagus.—Successful extirpation of cancer of the esophagus was performed in 1913. The 2 cases reported in that year remained a bold surgical adventure for a long time. Up to 1930 only 3 similar successes were reported. Recent advances in endothoracic surgery, according to Ferrari, led to successful extirpation of esophageal cancers; Garlock, Churchill and Phemister have reported impressive series of cases. Since 1940, extirpation of cancer of the thoracic esophagus has been done a number of times in Argentina; the first 2 of these patients are still well and now there are 5 more who have been saved from death by this procedure. The operation is not necessarily grave; its mortality is low and would be still lower if early operation were the rule. Two factors interfere with the successful surgical treatment of cancer of the esophagus: (1) The patient asks for medical advice relatively late and (2) the physician as well as the patient is hesitant in accepting the operation. Many physicians lack confidence in the merits of the operation, their attitude being much the same as that which prevailed thirty years ago with regard to rectal cancer. Today extirpation of rectal cancer is no longer disputed. In some respects extirpation of esophageal cancer is less difficult than that of rectal cancer. The esophagus is less septic and less vascular, and diffuse infection of the pleural cavity is avoided much more readily and better tolerated than that of the peritoneal cavity. Early clinical manifestations which permit earlier diagnosis, lesser malignancy and lesser tendency to metastatization are other factors that make the problem of esophageal cancer less serious than that of rectal cancer. Ferrari stresses that the possibility of esophageal cancer should be considered in the presence of dysphagia. Such patients should be referred at once to a center where thorough examination by roentgenography, esophagoscopy and biopsy is possible.

Revista de Neuro-Psiquiatría, Lima

5:315-431 (Sept.) 1942. **Partial Index**

*Acute Cerebral Edema After Neoarsphenamine Therapy. L. D. Espejo and J. Voto-Bernales.—p. 315.
Experimental Catalepsy Produced by Nicotine. C. Gutiérrez-Noriega.—p. 323.

Acute Cerebral Edema.—According to Espejo and Voto-Bernales acute cerebral edema after neoarsphenamine therapy is a rare but a grave complication. The condition may develop as a reaction of the nervous tissue to neoarsphenamine when the injection is given too rapidly and in the presence of an individual predisposition, as well as in certain diseases and infections. A constitutional vasomotor instability, especially in young persons, hyperthyroidism, toxic goiter, thymolymphatic disorders and alcoholism are the most frequent predisposing factors. The author reports 3 cases. The total dose reached before the appearance of acute cerebral edema was 0.9 Gm. or more. The symptoms appeared after the third injection in all of the cases. The prodromal symptoms consisted of acute headache, vomiting, epigastric pain, diarrhea, insomnia and incapacity for work. The acute symptoms were those of the apoplectic, convulsive and pseudoepileptic type. There was definite dissociation of the albumin component of the cerebrospinal fluid and increase in glycogen in all cases. The precipitation curve of the colloidal benzoic test was carried out in only 1 case. It was of the left (parenchymal) type. Two of the patients aged 28 presented vasomotor disorders. One was cured. The authors believe that acute cerebral edema after neoarsphenamine therapy is a local allergic phenomenon.

Book Notices

Manual of Oxygen Therapy Techniques Including Carbon Dioxide, Helium and Water Vapor. By Albert H. Andrews Jr., M.D., Director, Oxygen Therapy Department and Assistant Attending Otolaryngologist, St. Luke's Hospital, Chicago. Cloth. Price, $1.75. Pp. 191, with 33 illustrations. Chicago: Year Book Publishers, Inc., 1943.

In the preface Dr. Andrews points out that "correct administration of oxygen therapy requires attention to many details which are overlooked so frequently that a manual of this type has been considered necessary." The result appears to be an excellent compendium of a considerable amount of useful information not otherwise readily available to the technician, the nurse or even the physician who has occasion to operate oxygen therapy equipment. It should be valuable to those specializing in inhalation therapy. Except for a short section on the physiology of respiration and rationale of gas therapy the manual has been limited to a discussion of the mechanical aspects and recommended safety precautions of administering oxygen. Instructions and descriptions are supplemented by numerous illustrations and charts. The author has been quite thorough in his description of technics for operating a wide variety of modern and generally accepted types of equipment and in many instances presents special instructions which are required for specific makes of equipment. The book also includes operating data useful to those interested in carbon dioxide therapy, helium-oxygen therapy and water vapor therapy. Suggestions for handling administrative and clerical details of oxygen therapy in hospitals are doubtless based on the author's own practical experience and should prove extremely valuable to others. A chapter is devoted to a description of the organization and activities of an oxygen therapy department within the hospital. Another chapter describes various charts and records used for the recording of patients' progress and for the accumulation of statistical results of gas therapy. There are also chapters containing descriptions of and suggestions affecting the purchase of therapeutic gases, pressure regulating devices and gas piping systems as well as useful hints on the handling and maintenance of oxygen equipment. Though already widely used in the treatment of many different diseases and conditions, oxygen therapy seems on the way to still greater use, and this book should contribute much toward its effective, safe and economical application, without which oxygen therapy becomes merely a medical gesture.

Biochemistry and Morphogenesis. By Joseph Needham, F.R.S. Cloth. Price, $12.50. Pp. 787, with 328 illustrations. New York: Macmillan Company; Cambridge: University Press, 1942.

The printing of this book in Great Britain amid the disruption caused by a world war shows definitely that the British set a high and proper value on the maintenance of facilities for publishing an important scientific work not directly related to the war effort. The book is a painstaking analysis of the biochemistry of the morphogenic hormones in a search for a physicochemical causal basis for morphogenesis. As such it comes as a suitable supplement to the author's earlier three volume Chemical Embryology, in which the discussion was limited largely to the consideration of paracrystalline aggregates, colloidal miscelles, fibrous macromolecules and protein structure and the study of the chemical changes which go on in embryonic development.

Of the three parts into which the present book is divided, part I is devoted to the morphogenic substratum, including under this head such topics as the constitution of the egg of invertebrates and of vertebrates, particularly the hen's egg, environmental factors, mortality curves, embryonic nutrition and the mammalian placenta. Part II, dealing with the morphogenic stimuli, occupies the major part of the book. At this point the author's apology "on the part of one whose training was not morphological" seems quite unnecessary in view of the author's adequate presentation of the morphologic background. This part of the book discusses the general concepts of causal morphology and the extent to which biochemistry can be utilized as a source of causal factors in development. The evidence for the presence of organizers under various circumstances is fully treated, including the relation of organizers to genes and their possible role in carcinogenesis. Of the special technics employed, mention should be made of the successful use of a refinement of the cartesian diver manometer in the determination of oxygen consumption in small pieces of embryonic tissue. Part III, concerned with the morphogenic mechanisms, deals with the facts and theories of dissociability, heterauxesis, respiration, metabolism and polarity. The basic aim of the book as a whole is to show that organizing relations exist at the molecular and paracrystalline levels as well as at the morphologic levels; that chemistry and morphology are closely related. The usefulness of the book is heightened by its clear, concise English and by the inclusion of a glossary of terms, a bibliography of seventy pages, a general index and separate indexes of animals, plants and genes.

Radio Broadcasting: A Critical Study of Health Education by The Medical Profession, The Official Health Organizations, The Voluntary Health Agencies. Paper. Pp. 81. New York: New York Academy of Medicine, 1942.

This study was made under the supervision of the Committee on Medical Information of the New York Academy of Medicine with the aid of a grant from the Rockefeller Foundation, Division of Humanities. The study is divided into a chapter on background facts, one on opinions of experts gathered by personal interview, a chapter on critical study of the radio health education program of the New York Academy of Medicine called "Highways to Health," an interpretation of the opinions expressed by the experts, an evaluation of the data gathered from the study of the academy broadcasts, a chapter on the objectives of radio health education, one on technics in radio, one on the radio audience, one on radio and the printed word, one on the economics of radio health education, and a summary and conclusions.

The author presumably considers that, in general, health education by radio is not a success but that it could be made successful. This conclusion is based on the opinions of the experts whose names are listed in an appendix and who constitute in truth an impressive list of personalities in medicine, public health, radio and educational circles. Impressive as this list is, it adds nothing to the report because the reader cannot tell what any of these eminent persons actually contributed, since each is identified only by one star, two stars or three stars representing respectively the opinion that radio in health education is virtually valueless, that radio in health education does fairly well but could do better, that radio as an instrument of health education is doing very well indeed. If an eminent authority in public health with little or no radio experience is to be accepted at the same value as one who knows much about radio and little about health education, such a classification might be acceptable; but any one who is experienced in both radio and health education will not be satisfied by any such ambiguity.

The author is particularly critical of those who believe that it is necessary to attract audiences by radio presentations which have some of the features of commercial programs, namely entertainment. In the introduction he refers contemptuously to this idea: "cap and bells make a poor miter for the teacher's toga." Throughout the report he appears to be sharply critical of any one who would attempt to lure the radio audience with any of the bait to which this audience is so susceptible. Although he points out that studies by Lazarsfeld of the Columbia School of the Air indicate that the lower the scale of culture in the home the greater the amount of radio listening, he scorns the idea of appealing to these nonintellectual listeners with the daytime serials so dear to their hearts. He overlooks completely the fact that, no matter how excellent may be the educational material presented, it will be of little use if the only audience is the little man who wasn't there.

The purpose of drama, Dr. Schultz totally fails to recognize, is not to convey health information but to make reasonably sure that some one will be listening when the health education is conveyed. Dramatization will accomplish this, as demonstrated by the radio programs of the American Medical Association, to which audience response when asked is so great that it can seldom be asked for fear of overwhelming the resources available for handling and replying to audience mail.

The author would like to divide health agencies neatly into three groups, the voluntary health agencies whose primary purpose is to agitate and to campaign, the medical organizations whose function is to instruct from the heights of Olympus, and the health departments and other governmental agencies which can do a little of each. He believes that a medical society has no right to view with alarm, whereas a tuberculosis association or a health department may properly get excited about bad health conditions in the community! He divides the radio audience into numerous groups and goes so far as to advise that radio presentations should be aimed at specific groups rather than at wide audiences. Although he mentions the necessity for correlating radio with other health education activities, he treats radio throughout as if it were expected to accomplish the whole job of health education by itself, whereas it is in fact merely an attention catching medium which serves its most important function by attracting attention of indifferent persons and stimulating in them a desire to know something more about a subject important to them though not previously interesting.

The author says that dramatization is unwieldy and costly and that it obscures the educational purpose in radio health programs. Properly handled dramatization does none of these things. It is not unwieldy and need not be costly if community cooperation and ingenuity are appropriately substituted for dollars. With the author's contention that much interview and conversation are but shoddy imitations of genuine give and take on the air, this reviewer is in hearty accord. With the author's statement that a good health talk is better than a poor dramatization there can be no honest disagreement. But the fact remains nevertheless that good radio dramatizations interwoven with information have attracted the attention of millions of listeners who would otherwise have given no attention whatever to health talks or even interviews.

The most important points in this study are those which concern the defects and limitations of radio presentations, especially radio talks. These have too often been hastily and carelessly prepared and poorly delivered. The apparent but fictitious "expenselessness" of radio broadcasting has led to indifference and neglect in the preparation of radio material as compared with the care and expense lavished on printed matter and visual aids in health education. The author's recommendation for community cooperation in radio broadcasting looking toward better coordination of the quantity, quality and proportion of radio material broadcast in a given community is sound.

There are numerous criticisms in the report which are leveled at individual abuses. Since these abuses are not general, such criticism should either have been omitted or made specific. A case in point is the following: "Some medical societies are putting on dramatic programs which burlesque and belie medical research and which attempt to persuade the public that the doctor is a sort of hybrid Horatius at the Bridge and the humble St. Francis." The accusation is leveled at medical societies in plural. This reviewer, who is reasonably familiar with the national situation, knows of but few such instances. Other medical societies not guilty of this sort of thing should not have the finger of scorn pointed at them.

Texto de bacteriologia. Por los doctores Arturo Curbelo y Hernandez y Giraldo Insua y Cartaya, profesores auxiliar y agregado de la Catedra de bacteriologia de la Escuela de medicina de la Universidad de La Habana. Cloth. Pp. 610, with illustrations. Habana, Cuba: M. V. Fresneda, 1943.

This excellent book combines the usual subjects included in general bacteriology with those of infection and resistance. The book is written for students. The authors describe the subjects with great clarity according to established facts. The presentation is excellent, the printing is clear, most of the illustrations are new and the diagrams are didactic. The chapter on Rickettsia, probably the best, reveals familiarity with the subject, certainly not surprising, since typhus fever has been studied in Cuba since 1938.

One would like to see this book improved and enlarged in further editions. The reader may indulgently smile when in the listing of highlights in the history of bacteriology the authors quote the finding of bacillary dysentery in Cuba next to the discovery of sulfonamide compounds and the crystallization of tobacco mosaic virus, but this attitude may change in other passages of the book. The question of size of filtrable viruses—which poses basic problems concerning their nature—is dismissed with the statement that for most of them it ranges between 20 and 40 millimicrons; the filtrability of tubercle bacilli is accepted without much discrimination; too much space is devoted to aggressins, possibly just a word to designate a heterologous group of substances. Important phenomena such as the Shwartzman phenomenon are not mentioned.

The sources of the book are almost exclusively American, i. e. North American. Yet for the first time in a book on bacteriology the reader comes frequently across names and contributions from Latin America, some known, like Finlay's, others still obscure for most readers, like the group of Mexican and Cuban workers responsible for establishing the spirochetal etiology of Pinto's disease. In this respect the book is representative of the newer trends of scientific thought in Latin America, which, in quest of information, is swinging from the old to the new continent.

Understand Your Ulcer: A Manual for the Ulcer Patient. By Burrill B. Crohn, M.D., F.A.C.P., Associate in Medicine, Gastro-Enterology, Mount Sinai Hospital, New York. Cloth. Price, $2.50. Pp. 199, with 19 illustrations. New York: Sheridan House, Inc., 1943.

In line with the present tendency to give the layman an opportunity to know something about many ailments, Dr. Crohn presents a short description of peptic ulcer. The well known role of acidity, the bad effects of excessive or even ordinary smoking, the influence of psychic upsets or mental strain, the tendency toward recurrence of the ulcer, seasonal influence, the part played by age and occupation and the clinical course are well described not alone for the layman but also for the physician. If any criticism should be leveled at the treatment of the subject it might be that too much attention has been placed on the description of the pathology and x-ray examination, which are not well comprehended by the layman. The discussion of the various methods of treatment of ulcer is well presented and its value is enhanced by part II, which is an appendix on diets by Sylvia Bayard, consulting dietitian. Here are mentioned lists of foods allowed and to be avoided and the manner of preparation of the diet adequate for treatment of ulcer. It would not be amiss for the practitioner to acquaint himself with this section of the book. The makeup of the book is excellent and its value improved by several illustrations. It can serve a good purpose for the layman and nurses or even for some physicians.

Sanitary Inspector's Manual, Louisiana State Department of Health, New Orleans, La. [Including] Supplement I: Act 142 of 1936 as Amended by Act 185 of 1942, The State Food, Drugs and Cosmetic Act; Supplement II: Act. No. 202 of 1942, Enrichment of Flour and Bread; Supplement III: Act. No. 203 of 1942, Enrichment of Oleomargarine. Prepared, 1942, by Ben Freedman, M.D. Paper. Pp. 350; 22; 8; 2, with illustrations. New Orleans, Louisiana: Peerless Printing Co., 1942.

For use of sanitary inspectors of the Louisiana State Department of Health, the author has compiled a manual covering every phase of the sanitarian's work. The chapters include bacteriology, bacteriology of water and milk, control of food and milk supplies, sewage disposal, food handling, meat control and the control of rodents and insect pests and of communicable diseases. There are sections on housing, vital statistics and numerous formulas. Special supplements cover the legislation of the state of Louisiana affecting the work of the sanitarian. A number of supplements are also included from official publications of the American Public Health Association. The work is so practical that its immediate application to the duties of the sanitarian is obvious. A similar publication for sanitarians in other states, modeled on this publication, will be well worth while.

Heating Your Home in Wartime for Comfort, Economy, Health. A Bulletin Prepared for Governor Harold E. Stassen by the Scientific Advisory Committee to Minnesota War Industries. Paper. Pp. 32, with 5 illustrations. St. Paul: Minnesota Resources Commission, 1942.

This pamphlet contains information about heating the home. It is written in a popular style with brief descriptions of different methods for avoiding heat loss from structures and for saving fuel by modification of operating conditions. A brief discussion of comfort and health factors in relation to house heating is also included.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

COMMON COLD, ATYPICAL PNEUMONIA AND SULFONAMIDE ADMINISTRATION

To the Editor:—**For the past several months I have observed many cases of acute respiratory infection which did not conform with the ordinary chest cold that have been seen so frequently in the past. In talking with other physicians in this neighborhood I find that they also are experiencing this peculiar type of respiratory infection. One of the unusual things about these cases is that a large number of them are associated with moderate hemoptyses. It has been called to my attention that most of these cases in which hemoptyses occurred were also cases in which a sulfonamide drug had been administered. In view of this finding I am beginning to be curious as to the possibility of the drug being in some way responsible for the hemoptyses.** W. L. Howard, M.D., Battle Creek, Mich.

ANSWER.—In the absence of any details describing the acute infection of the respiratory tract referred to, which seems to differ from the ordinary "chest cold," one could guess that the query deals with the newly recognized syndrome called "primary atypical pneumonia" or "viral" pneumonia, which has assumed epidemic proportions in recent months, particularly in military camps. However, hemoptysis, although it may occur, is not particularly characteristic of this infection. There is no reason to suppose that the use of sulfonamide compounds is connected with the spitting of blood in such cases; at least, no mention of it has as yet appeared in the literature. The question may be asked why sulfonamide compounds were given to such patients at all.

The query touches on the controversy concerning the use of sulfonamide compounds routinely for the common cold either in the hope of influencing the disease itself or to prevent the development of pneumonia. Convincing evidence has not yet appeared to show that the indiscriminate use of sulfonamide compounds is helpful in the common cold, and all authors agree that they have no effect on the syndrome called viral pneumonia, yet they are widely used for both conditions. In the state of present knowledge there is no justification for the use of chemoprophylaxis in colds to prevent pneumonia. In the first place only about 1 in 1,000 patients with colds develop clinical pneumonia, and not all pneumonias which so develop are amenable to chemotherapy. Thus far in the current season, for example, from 60 to 75 per cent of pneumonias have been of unknown cause. The mortality rate in these cases was nil even in those untreated with sulfonamide compounds. Secondly there is incomplete knowledge at present as to the incidence and degree of sensitization to sulfonamide compounds after they are given empirically in trivial diseases, which may cause a dangerous reaction if chemotherapy is given later for a really serious infection in which it is urgently needed. There are, no doubt, certain selected cases of the common cold in which chemoprophylaxis seems to be indicated: (1) in severe cases with fever and symptoms which show a tendency to increase with increasing leukocytosis and evidence of spread into the bronchi and lungs, (2) when an epidemic of pneumococcic pneumonia or meningococcic meningitis coexists and, according to Spink (Use and Abuse of Chemotherapy, *Minnesota Med.* **25**:988 [Dec.] 1942), (3) in patients who have valvular heart disease and (4) in obstetric patients who develop colds at or near term.

In the average case of the common cold an alert physician by clinical observation alone can usually decide whether or not to withhold chemotherapy until actual indication for its use arises. His judgment is greatly aided by roentgenography when available and by laboratory studies to discover the cause. With regard to the latter point it is evident from the studies of Faller, Quickel and Smith (*Pennsylvania M. J.* **46**:339 [Jan.] 1943) that physicians in general are deplorably indifferent. In their survey, attempts to discover the causative agent, by which the selection of specific therapy can be controlled, were made in only 17 per cent of cases of pneumonia.

OZENA

To the Editor:—**A patient has ozena. Will you kindly send me the treatment for this condition?** A. A. Lepis, Lieutenant, M. C., A. U. S.

ANSWER.—There is no completely satisfactory or even simple answer to the query. First of all one must consider the numerous notions regarding the causation of ozena, if one means by that term an atrophic rhinitis accompanied by crusting and a fetid odor. Cullom in a recent article mentions at least ten theories concerning etiology. Among these are

1. Too great shortness and width of the nostrils.
2. Purulent rhinitis of childhood.
3. Purulent disease of the nasal accessory sinuses.
4. Infection due to specific bacteria such as (*a*) Bacillus mucosus (Abel), (*b*) Bacillus fetidus ozenae (Hajek), (*c*) Coccobacillus fetidus ozenae (Perez). The following may be added: (*d*) endocrine disturbances and vitamin deficiencies.

Each proponent of a theory bases his therapy in large part on what he considers to be the chief causative factors. This leads some to stress the treatment of a concomitant purulent sinusitis, others to the giving of various vitamins and still others to the use of various endocrine preparations. In this connection it may be wise to mention Crowe's warning that estrogenic injections and implants for the treatment of ozena in the young may cause harmful disturbances in the long bones and genitalia which outweigh any nasal benefits. Modern conservative treatment may be summed up as follows: Surgical procedures which aim to narrow the nasal passages should be reserved for those cases which resist all simpler measures. Purulent sinusitis should be searched for and if present should be handled according to accepted standards.

The patient's general health should be considered; the nasal cavities should be thoroughly cleansed in the office by the removal of crusts and secretion, and the patient may be instructed in the use at home of saline irrigations and douches. Following this, some bland vegetable oil such as oil of sesame may be sprayed in the nose. Mineral oils should be avoided so as not to risk the possibility of lipid changes in the lungs. Iodine in glycerin in strengths varying from 1 to 5 per cent is used by many as drops in the nose or applied with a swab; scarlet red as a 5 per cent ointment is recommended by some, and still others use 10 to 20 per cent dextrose solutions in glycerin as drops to abate the objectionable odor.

References:

Cullom, M. M.: Ozena, THE JOURNAL, Sept. 20, 1941, p. 987.
Lederer, Francis L.: Diseases of the Ear, Nose and Throat, Philadelphia, F. A. Davis, 1938.

POSSIBLE LATE COMPLICATIONS OF ANAPHYLACTIC REACTION

To the Editor:—**A patient who has been a laborer all of his life, now aged 65, has been in good health as far as he is aware. On Aug. 7, 1942 he smashed the second and third fingers of his right hand between a stone and the rear of a truck. He was sent to the office of a doctor, who, after dressing the injured fingers, gave him two intramuscular injections of antitoxin, one in the arm and one in the buttock—from what I understand they were to prevent tetanus. On his way home he began to vomit and have chills. He went to bed; the next day his eyes began to swell and he had a generalized urticaria. The chills and later fever continued for three days, and the urticaria subsided soon thereafter. He has remained in bed off and on since then. I examined him at his home on September 27, when he complained of generalized muscle pain and weakness, severe pain in the injured hand, occasional dizzy spells, loss of appetite and strength, irritability and nervousness. Objectively he appeared to be weak and apprehensive. There was a generalized muscle tenderness on deep pressure, moderate swelling and thickening of the terminal phalanges of the injured fingers but no evidence of any infection, a fine tremor of the eyelids, tongue and fingers, and increased knee jerks. The blood pressure was 200/100, the pulse rate 64, the heart sounds were distant but regular with a systolic murmur at the apex, the heart was not enlarged and there was generalized arteriosclerosis. The blood Wassermann reaction was negative, blood sugar 73 mg., nonprotein nitrogen 27.9 mg. Present examination reveals that his general condition is about the same as that reported. There is no question in my mind that the hypertension and the arteriosclerosis existed prior to the injury to the right hand and the anaphylactic reaction following the injection of the antitoxin; but here is a man who did laboring work all his life and apparently was in good physical condition, who, following the occurrences mentioned, is today totally disabled. My purpose in sending this information is to ascertain what effects on anaphylactic reaction would have on his preexisting condition. Is there any literature that would aid me in this matter?** P. F. Cardinale, M.D., Elizabeth, N. J.

ANSWER.—It is not entirely certain from the facts at hand whether the patient had an accelerated form of serum sickness or an immediate type of serum reaction due to a previously existing sensitiveness. In either type of reaction a number of complications have been described. It is possible for the anaphylactic type of reaction, whether due to serum or to other antigens, to result in various profound responses such as abortion, pronounced gastroenteritis, protracted nervous and toxic states and interference with the normal functions of the liver, kidneys and blood vessels. Serum sickness has been not infrequently reported to cause neurologic complications and particularly neuritis. Among other occasional effects that have been noted as a result of serum sickness may be mentioned edema of the larynx, abdominal pain, gastrointestinal hemorrhage, local purpura, hematuria, jaundice, liver atrophy, optic neuritis, laryn-

geal nerve paralysis, Ménière's syndrome and psychoses. There is no doubt that the patient in question had a preexisting arteriosclerosis and hypertension. This abnormal vascular state may have been the underlying basis favoring the results that followed the serum reaction, but it must be appreciated that it is possible perhaps for similar effects to be produced without any previously existing organic states.

References:

Doyle, J. B.: Neurological Complications of Serum Disease, *Am. J. M. Sc.* **185**: 484 (April) 1933.
Wilson, George, and Hadden, S. B.: Neuritis and Multiple Neuritis Following Serum Therapy, THE JOURNAL, Jan. 9, 1932, p. 123.
Wadsworth, G. H., and Brown, C. H.: Serum Reaction Complicated by Acute Carditis, *J. Pediat.* **17**: 801 (Dec.) 1940.
Patrassi, Gino: Serum Sickness of Central Nervous System, *München. med. Wchnschr.* **87**: 1176 (Oct. 25) 1940.

DIAGNOSIS OF TYPE OF ANEMIA

To the Editor:—**A woman aged 77 has an anemia with 2,438,000 red blood cells and 40 per cent hemoglobin. Neither blood smear nor color index is indicative of pernicious anemia. She has a chronic valvular heart disease with no decompensation, a blood pressure of 100/60 and normal urine. The vaginal examination is negative except for prolapse of the uterus. From the history and examination I was unable to find any place where she could be losing blood except a history of vomiting blood four years ago. Later x-ray examinations of the gastrointestinal tract were negative, and she has not lost weight since. What type of iron and liver therapy is indicated? Considering her age and the myocardial damage, is a blood transfusion advisable?**

M.D., Pennsylvania.

ANSWER.—It would not be possible to say what type of therapy is indicated until the anemia is carefully classified as to morphology and etiology. The mainstay in the differential diagnosis of such an anemia is the laboratory examination. Such determinations as the volume index, saturation index, icterus index, reticulocyte count, platelet count and a careful study of the blood smear should give a clue as to the type of anemia. Further studies, such as sternal puncture with examination of the bone marrow, stool examinations and renal function tests, may also be necessary.

The age of the patient and the condition of the heart are not contraindications to giving a blood transfusion. However, if the type of anemia is such that it would respond to specific therapy, transfusions would not be necessary.

References to classifications and the laboratory diagnosis of anemia:

Osgood, E. E.: Laboratory Diagnosis, Philadelphia, Blakiston Company, 1940.
Wintrobe, M. M.: Clinical Hematology, Philadelphia, Lea & Febiger, 1942.

COBRA VENOM FOR ANALGESIA

To the Editor:—**In the *Journal of International College of Surgeons* (3: 357 [Aug.] 1940) Paul Butler, of Orlando, Fla., makes the following assertions as to the remarkable properties of snake venom. He maintains that "it has recently been proved that cobra venom has a higher analgesic action than morphine. . . . Believing, therefore, that the analgesic effect of snake venom and its value in therapeutics cannot alone explain its curative effects . . . and that the evidence indicates a deep effect on the metabolic processes in the human body . . ." I looked through the pages of New and Nonofficial Remedies, and the only reference to snake venom concerned Lederle's moccasin for hemorrhage (not recommended). Butler appends two references: Burkhardt, Albrecht: Treatment of Rheumatic Disorders with Snake Venom, *Deutsche med. Wchnschr.* 61:1159 (July 19) 1935, and Spangler, R. H.: Intramuscular Injection of Foreign Protein: Crotalin in 300 Cases of Epilepsy, *New York M. J.* 107:727 (April 20) 1918. I should like to know if there is any truth in Butler's contention. Has any experimental work been done of sufficient value to entitle it to deserve his encomiums? It seems to me from the paucity of literature that there has not.**

Thomas I. O'Drain, M.D., Philadelphia.

ANSWER.—The use of cobra venom in clinical therapeutics has been developed in the last eight years by both American and foreign investigators. The most prominent publications from French writers were those of Charles Taguet (*Bull. et mém. Soc. méd. d. hôp. de Paris* **137**:310 [April 29], 651 [Dec. 8] 1933) and Albert Calmette and A. Orticoni (*Presse méd.* **42**:112 [Jan. 20] 1934).

In this country practically all of the publications have been by Macht and his collaborators (Macht, D. I.: *Proc. Nat. Acad. Sc. U. S.* **22**:61, 1936. Macht, D. I., and Spencer Elizabeth C.: *J. Am. Pharm. A.* **31**:146 [May] 1942). The last mentioned is his most recent publication. Other investigators in India and in Argentina have also studied the analgesic effects of cobra venom. According to Macht and his collaborators, cobra venom injected in small doses produces analgesia and therefore suitable preparations were first employed for the relief of intractable pain suffered by patients with malignant disease. Macht maintains that he has shown experimentally that this relief of pain is not due to a peripheral effect on the nerve endings or nerve fibers but to a direct action of the drug on the brain, and the hypothalamus is the center of the cobra venom analgesia.

Cobra venom solution was discussed in a preliminary report of the Council on Pharmacy and Chemistry (THE JOURNAL, Oct. 5, 1940, p. 1196). It was concluded that purified cobra venom is of some value for the relief of pain, especially that of inoperable cancer (its use in the early stages would tend to delay curative measures); that it does not displace morphine completely in more than relatively few cases but it is of value in these few; that it appears to be of limited value in the treatment of trigeminal neuralgia and the various conditions commonly grouped loosely under the names of "rheumatism" and "arthritis"; that its therapeutic effects are variable and uncertain in all painful conditions; that the disagreeable side actions, including nausea, vomiting, diarrhea and pain of injection—even intense pain at times, mentioned in medical journals—must be brought to the attention of those who use cobra venom; that it must not be recommended for those who are severely ill except those suffering from inoperable malignant tumors or from incurable disease; that the optimum dosage (after the first single dose) remains to be determined, and that the effects are not immediate but may take hours to appear.

CHOREA WITH EMOTIONAL BEHAVIOR DISTURBANCE

To the Editor:—**Two years ago I saw a girl aged 12 with chorea. After intramuscular magnesium sulfate injections and several hyperthermic treatments she apparently made a recovery, and I lost sight of her. Now her mother states that she developed the present symptoms within the past year. She has some purposeless explosive movements, the most distressing of which is a sudden explosive speech outburst, during which the patient suddenly uses vulgar or curse words. During conversation she will talk quite intelligently but in the middle of a sentence she will suddenly say "G—— d——" and then proceed to finish the sentence; also while sitting quietly she will suddenly explode in this manner. The patient does not seem to be psychotic. She lives quietly at home with her grandparents. Her mother works. The patient realizes that this condition is abnormal and expresses a real desire to get well so that she can attend school, go to shows and otherwise mingle with others. I shall appreciate any suggestions you may have to offer along the line of treatment. The parents are too poor to afford a special school for the girl.**

M.D., Arkansas.

ANSWER.—The patient has a recurrence of chorea with emotional behavior disturbances. The latter occurs in a mild way in many cases of chorea. The use of vulgar or curse words in this disease is not rare. The possibility of a degenerative or Huntington's chorea must be thought of, although it is improbable because of her age. The following treatment is suggested: The patient should have absolute rest in bed for six weeks in a darkened room. No visitors and no exciting radio stories or plays should be allowed. One and the same person should act as nurse. The patient should sleep alone in her room. She should eat alone. She should sleep from fourteen to sixteen hours daily. Solution of potassium arsenite in doses of 5 to 7 drops three times daily can be given for thirty days or 5 grains (0.3 Gm.) of acetylsalicylic acid three times daily for twenty days. Lukewarm baths for twenty minutes, once daily, can also be given for its sedative effect. Insomnia may be treated by bromides or phenobarbital. The heart should be studied to rule out an associated endocarditis.

OVARIAN NEOPLASM

To the Editor:—**I should like to take exception to the form of treatment as outlined in Queries and Minor Notes in the Jan. 30, 1943 issue under the heading "Probable Ovarian Neoplasm." Under the description of the patient's pelvis there is apparently a cervical polyp or other neoplasm partially extruded from the uterus into the cervix. Laparotomy, regardless of the associated conditions, almost without exception should be postponed until the intrauterine and intracervical tumors are removed by the vaginal route. When submucous myomas have been partially or completely extruded through the cervix, they are almost always infected, and laparotomy carried out in these conditions is hazardous. In this particular case it would appear to me to be advisable to remove the intracervical tumor, await the closure of the cervix and then perform the necessary abdominal procedure.**

C. D. Berry, M.D., Orlando, Fla.

WASHING HYPODERMIC NEEDLES TO PREVENT CLOGGING

To the Editor:—**In doing intradermal tests for allergies there results the problem of washing out each needle so that the test solutions do not become contaminated. I have devised a neat, quick way of washing out our needles. The needles are stuck into the lumen of a piece of old duodenal tube. When the tube is clamped shut on one end and a luer syringe applied to the other end, alcohol can be swished in and out through the needles, thereby cleaning them thoroughly. The needles are then left sticking in the tube, as this is an excellent place to keep them until next used.**

Anton W. Oelgoetz, M.D., Columbus, Ohio.